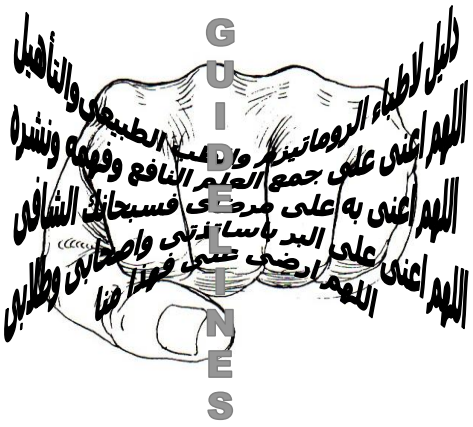
GUIDELINES

for some Rheumatic disorders



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Guidelines for management of some Rheumatic diseases

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For the author
Elements of Rheumatology
Therapy of rheumatic diseases
Periodic currents of Egyptian Rheumatology Group
Therapy of Rheumatic disorders
Bursitis
Knee Pain Syndormes

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Section (I)

Guidelines & Criteria for Individual disorders

Ankylosing Spondylitis

Before diagnosis of Ankylosing spondylitis (AS) , you may use criteria for classification of seronegative spondyloarthropathy (SpA) to classify your patient as having one of the group members , then you may use criteria for classification of AS

Seronegative Spondyloarthropathies

Before discussing the classification criteria for Spa , we may first define the members of the group & what are the clinical & investigational characters of this group of disorders which are first defined by Wright & Moll from Holland in 1976

Members of the group :

Diseases belong to Seronegative Spodyloarthropathies (SpA)

- Ankylosing Spondylitis (AS)
- Psoriatic Arthropathy (PsA)
- Rective arthropathy (ReA) & Reiter,s Syndrome (RS)
- Arthropathy of Inflammatory Bowel Disease (IBD)
- Undifferentiated SpA-ies
- Juvenile chronic arthritis (Juvenile onset Ankylosing Spondylitis { AS })

Clinical Characteristics of Spondyloarthropathies

1- Typical pattern of peripheral arthritis (LL , Oligo , Asymm.)
2- Tendency to radiographic sacroiliitis

3- Absence of Rheumatoid factor
4- Absence of SC nodules & other extra-articular features of RA
5- Overlapping extra-articular features characteristic of the group (uveitis)
6- Significant familial aggregation
7- Association with HLA-B27

Moll & Wright 1976

Classification Criteria for Spondyloarthropathies

To classify a patient as suffered from one of the members of SpA

These criteria , although clearly not intended for diagnostic purposes , might be useful for identification of atypical & undifferentiated forms of SpA .

Two set of criteria for classification of SpA :
1- Amor criteria &
2- European Spondyloarthropathy Study Group (ESSG) criteria

Amor Criteria … 1990

The first set of classification criteria based on case-controlled examination of the entire SpA family

A- Clinical Symptoms or Past History

1- Lumbar or dorsal pain during the night or morning stiffness of lumbar or dorsal (1)
2- Asymmetric oligoarthritis (2)
3- Buttock pain (1) … Alternating buttock pain (2)
4- Sausage-like toe or digit (2)
5- Heel pain (2)
6- Iritis (2)
7- Nongonococcal urethritis or cervicitis (1)
8- Acute diarrhea (1)
9- Presence or history of psoriasis , balanitis or IBD (2)

B - Radiologic Finding

10- Sacroiliitis (grade > 2 if bilateral ; grade > 3 if unilateral) (3)

C- Genetic background

11- Presence of HLA-B27 or family history of AS , RS , uveitis , psoriasis or chronic IBD (2)

D- Response to Treatment

12- Clear-out improvement of rheumatic complaints with NSAIDs in less than 48 hours or relapse of the pain in less than 48 hours if NSAIDs discontinued (1)

If the patient get score 6 or more , could be classified as SpA

The second set

ESSG Criteria 1991

In contrast to Amor criteria , the ESSG criteria used only two entry parameters

According to this classification , patients should be evaluated if they have one of the following :

1- Inflammatory spinal pain
2- Synovitis (that is asymm. or predominantly of the L.L.)

A patient is considered to have SpA if one of the above is present , plus any one of the following features :

1- Positive family history
2- Psoriasis
3-IBD
4-Nongonococcal urethritis or cervicitis , or acute diarrhea
within 1 month before arthritis
5- Buttock pain alternating between right & left gluteal areas
6- Enthesopathy
7- Radiographic SI

Comments on the criteria of ESSG

Let us discuss some details about each criterion & how to differentiate ?

Entry for diagnosis in ESSG criteria
Spinal pain (Inflammatory)
Characteristic Synovitis

The inflammatory spinal pain should be :
> 3 months
Before 45 years
Insidious onset
Improved by exercise
Associated with morning stiffness

Synovitis , It shoud be :
Inflammatory = arthritis (not mechanical)
Oilgoarticular (less than 4 joints)

Asymmetrical
Lower extremities

Family History
1 -- What degree ?
First & Second degree (parents & grand parents , brothers & sisters)
2 -- What diseases ? (ask about the following diseases)
AS
PsA
ReA & RS
Acute Uveitis
IBD

Psoriasis , psoriatic lesion should be diagnosed by :
By physician OR
By yourself

Inflammatory Bowel Disease
Not only diarrhea or disturbed bowel
Diagnosis by physician & confirmed by :
Radiological examination
OR
Endoscopy & histopathology

Recent infection
It should be Non-gonococcal , affecting Genitourinary OR Gastrointestinal Tracts
OR >
Urethritis
Cervicitis
Acute diarrhea
One month before musculoskeletal manifestations &
Confirmed by swab or culture

Buttock Pain
It is not highly specific , but if it is
Unilateral
Alternating
Atypical sciatica
It will be more specific

Enthesopathy
Where you have to look for enthesitis of SpA ?
Any where , but specifically it may affect
Plantar fascia
Achilles tendon
It is characterized by spontaneous pain OR tenderness at insertion of these locations

Sacroiliitis
It should be evident radiologically

These criteria , although not intended for diagnostic purposes , might be useful for identification of atypical & undifferentiated forms of Spondyloarthropathies before additional studies , such as radiography of SI joints or an HLA-typing test , are requested

if your patient fulfill classification criteria for SpA ,
Ask your self , to which member of the group your patient belong
The following criteria may help

Diagnostic strategy for Spodyloarthropathy :

- If your patient have inflammatory low back pain or oligoarthritis of lower extremity : The probability of SpA is **14%**
- If additional features from Amor OR ESSG criteria : the probability for diagnosis increase to (30) up to (**70%**)
- If HLA-B27 , Sacroiliitis or both : the probability increase up to **95%**

If your patient belong to the group & satisfy one of the two sets of criteria , use the other criteria specific for each member of the group

In the book you have , only two criteria are available (for Ankylosing spondylitis & reactive arthritis) , while others (Reiter,s Syndrome , Psoriatic Arthropathy & Inflammatory Bowel disease { Enteropathic athropathy }) , are not .

For diagnosis of undifferentiated SpA , , if your patient fulfill the classification criteria of SpA & does not fulfill criteria of other members , he may have undiff. SpA .

Criteria for diagnosis of Ankylosing Spondylitis

Modified New York , 1984 for diagnosis of AS

1- Low back pain of at least 3 months duration improved by exercise & not relieved by rest
2- Limitation of lumbar spine in sagittal & frontal planes
3- Chest expansion decreased relative to normal values for age & sex
4- Bilateral sacroiliitis grade 2 to 4
5- Unilateral sacroiliitis grade 3 to 4

Definite AS = unilateral grade 3 or 4 OR bilateral grade 2 to 4 sacroiliitis & any clinical criterion

The criteria of (limitation of motion of the lumbar spine) & (limitation of chest expansion) appear to reflect disease duration ; they are usually not present in early disease .
Indeed , it should be stressed that classification criteria are usually not well suited for early diagnosis of disease .

Diagnostic Features of Ankylosing Spondylitis

Consider a diagnosis of AS if there is :

1-Inflammatory spinal pain

- Onset before age 40
- Insidious onset
- Persistence for at least 3 months
- Morning stiffness
- Improvement with exercise

2-Chest pain
3-Alternative buttock pain
4-Acute anterior uveitis
5-Synovitis

- (predominantly of lower limbs , asymmetric)

6-Enthesitis

- (heel , plantar)

7-Radiographic sacroiliitis

8-Positive family history for :

- AS , Psoriasis
- Chronic inflammatory bowel disease

Guidelines for management of AS :

1- No cure , but most patients ca be well managed
2- Early diagnosis very important
3- Education of patient to increase compliance
4- Appropriate use of anti-rheumatic drugs primarily NSAIDs
5- Continuity of care
6- Daily exercise very important (e.g. swimming)
7- Sleep on firm mattress
8- Appropriate sports & recreation
9- Supportive measures & counseling
10- Avoidance of smoking
11- Avoidance of trauma (osteoporosis of the spine)
12- Patient support groups
13- Family counseling

Adapted from Khan MA , Skosey JL: Ankylosing spondylitis & related spondyloarthropathies . In Samtr M (ed) ; Immunologucal disease . Boston . Little , Brown & Co 1988 , pp 1509 – 1538 (cited by Linden et al , Kelley,s textbook of Rheumatology , 2005)

Sulfasalazine
It is effective in reducing synovitis in patients with peripheral polyarticular involvement but had no results on axial involvement

There is no convincing evidence that MTX works in AS
Leflunomide showed little efficacy in an open trial

Thalidomide
A sleeping pill with definite toxicity in pregnancy , administered orally has now been used in AS
The most prominent effects were reduction of ESR & CRP levels

Anti-TNF-alpha agents

1- Infliximab

3-5 mg / kg every 6 to 8 weeks after an initial saturation phase

2- Etanercept

25 mg subcutaneously two times each week
They improve the signs & symptoms of the active disease

Guidelines for the use of anti-alpha-directed therapies have recently been developed

(Maksymowych et al , 2003 & Braun et al , 2003 , covered by the same reference)

ASAS recommendation for the initiation of treatment with Biologics in patients with AS

Which patient ?

Diagnosis

- Patients normally fulfilling modified New York criteria for definite AS

Active disease

- For at least 4 weeks
- BASDAI > 4 (0-10)AND Expert,s Opinion (Initiation yes/no)

Treatment Failure

- All patients must have had adequate therapeutic trials of at least two NSAIDs
- An adequate therapeutic trial would be defined by :
- Treatment for at least 3 months at maximal recommended or tolerated anti-inflammatory dose unless contraindicated
- Treatment for < 3 months where treatment was withdrawn because of intolerance or toxicity or contraindicated
- Patients with symptoms peripheral arthritis (normally having or failing local steroid injection for those with oligoarticular involvement) must have had adequate therapeutic trial of NSAIDs & at least salazopyrine

- Patients with symptomatic enthesitis must have adequate therapeutic trial of at least two local steroid injections unless contraindicated

Contraindication

- Women who are pregnant or breast feeding , effective contraception must be practiced
- Active infection
- Patients at high risk of infection including :
  - Chronic leg ulcer
  - Previous TB
  - Septic arthritis of a native joint within the last 12 months
  - Sepsis of a prosthetic joint within the last 12 months
  - Persistent or recurrent chest infections
  - Indwelling urinary catheter
  - Multiple sclerosis

  - Malignancy or preliminary states excluding :
    - Basal cell carcinoma
    - Malignancies diagnosed & treated > 10 years previously

Anti-phospholipid Antibody Syndrome

Preliminary Classification Criteria for Antiphospholipid Antibody Syndrome (APS)

I - Clinical

Vascular Thrombosis

- One or episodes of :
- Arterial thrombosis OR
- Venous thrombosis OR
- Small vessel thrombosis , in any tissue or organ , confirmed by imaging OR Doppler studies or histopathologic studies . For histopathologic confirmation , thrombosis should be preset without significant evidence of inflammation in the vessel wall

Pregnancy morbidity

- One OR more :
- Unexplained deaths of a morphologically normal fetus at OR after he 10^{th} week of gestation with fetal morphology documented bu ultrasound or by direct examination of the fetus OR
- Premature birth of a morphologically normal neonate at or before the 34^{th} week of gestation because of severe preeclampsia , eclampsia or severe placental insufficiency OR
- Three or more unexplained consecutive miscarriage with anatomic , genetic , or hormonal causes excluded

II - Laboratory

Anticardiolipin antibody (aCL)

- IgG &/or IgM isotype present in medium or high titer on two or more occasions , 6 weeks or more apart , and
- Measured by a standard ized ELIZA for B2 glycoprotein I –dependent anticrdiolipin antibody
- Abnormality present in plasma on two or more occasions , 6 weeks or more apart &
- Detected according to the guidelines of the International Society on Thrombosis & Hemostasis Scientific Subcommittee on Lupus Anticoagulants-dependent antibodies .

Non-defining Clinical & Laboratory Features of the anti-phospholipid Antibody Syndrome

Clinical :

- Livedo reticularis
- Thrombocytopenia
- (usually 50.000 to 100.000 platelets / mm3)
- Autoimmune hemolytic anemia
- Cardiac valve disease (late finding)
- Multiple sclerosis-like syndrome & other myelopathy
- Monofocal neurologic symptoms
- Chorea
- Catastrophic vascular occlusion syndrome
- Pulmonary hypertension
- Systemic hypertension
- Renal failure

Laboratory

- IgA anticrdiolipin antibody
- Antibodies to pgosphatidylserine
- Antibodies to B2 glycoprotein I
- Proteinuria
- False positive test for Syphilis
- Hyperintense lesions on T2-weighted brain magnetic resonance imaging (MRI)

Preliminary Criteria for the classification of Catastrophic Antiphospholipid Syndrome (APS)

1- Evidence of involvement of three or more organs , systems or tissues
2- Development of manifestations simultaneously or in less than 1 week
3- Conformation by histopathology of small vessel occlusion in at least one organ or tissue
4- Laboratory confirmation of the presence of antiphospholipid antibody (aPL) (LA or aCL or antiB2-glycoprotein antibodies

Definite Catastrophic APS

- All four criteria

Probable Catastrophic APS

- Criteria 2 through 4 & two organs , systems or tissues involved
- Criteria 1 through 3 except no confirmations 6 weeks apart due to early death of patient not tested before catastrophic episode
- Criteria 1, 2 , 4

- Criteria 1 , 3 , 4 & development of a third event more than one week but less than one month after first despite anticoagulation

For criterion 1

- Usually clinical evidence of vessel occlusions confirmed by imaging techniques when appropriate
- Renal involvement is defined by a 50% rise in serum creatinine , severe systemic hypertension , proteimuria , or some combination of these

For criterion 3

- For histopathologic confirmation , significant evidence of thrombosis must be present , although vasculitis may coexist occasionally

For criterion 4

- If the patient has not been previously diagnosed as having APS , laboratory confirmation requires that presence of aPL be detected on two or more occasions at least 6 weeks apart (not necessarily at the time of the event), according to the proposed preliminary criteria for he classification of APS

Treatment Recommendations For Antiphospholipid Antibody Syndrome

Michael D. Lockshin , Antiphospholipid Antibody syndrome : Chapter 77 ; Kelley,s textbook of rheumatology , seventh edition , 1249-1257 , 2005

General principles : anticoagulation is the treatment for APS . Warfarin , Heparin , & low-molecular-weight heparin , often in association with low-dose aspirin are all used

Antibody titer	Clinical circumstances	Recommendations
Moderate or high positive	**Asymptomatic**	No treatment
	Equivocal thrombosis	Aspirin , 81mg/day
	Recurrent venous thrombosis	Warfarin INR 2.5 inefinitely
	Arterial thrombosis	Warfarin INR 2.5 indefinitely
	First pregnancy	No treatment

	Single pregnancy loss at least less than 10 weeks	No treatment
	Recurrent fetal loss or loss after 10 weeks , No thrombosis	Low dose heparin (5000 U bid) or low – molecular-weight heparin throughout pregnancy , discontinue 6 to 12 weeks postpartum
	Recurrent fetal loss or loss after 10 weeks , thrombosis	Therapeutic heparin or low-molecular-weight heparin throughout pregnancy , warfarin postpartum
	Livedo reticularis	No treatment
	Leg ulcer	Warfarin INR 2.5
	Valve nodules or deformity	No known effective treatment ; full anticoagulation if emboli or intracardiac thrombi demonstrated
	Thrombocytopenia of more than 50000/mm3	No treatment
	Thrombocytopenia less than or equal to 50000/ mm3	Prednisone up to 60mg/day
Absent or low positive	**Recurrent venous thrombosis**	Evaluate for proteinc , protein S or antithrombin III deficiency , factor V Leiden ; Warfarin , INR 2.0 to 3.0 indefinitely
	Arterial thrombosis	Evaluate for homocystinemia , atherosclerosis , vasculitis , Warafarin 2.5 indefinitely
	Recurrent pregnancy loss	Evaluate for other coagulopathies , other causes of pregnancy loss ; comsider heparin , 5000 U bid or low-molecular-weight heparin throughout pregnancy ; discontinue 6 to 12 weeks postpartum

Anticoagualtion is indicated for seropositive patients with thrombosis & at the diagnosis of pregnancy in a seropositive women who had had prior pregnancy losses attributable to APS

Behcet's Disease

International Study Group Criteria for Diagnosis of Behcet's Disease

The diagnosis of Behcet,s disease is sometimes difficult to confirm , particularly in patients with partial symptomatology

Clinicians & investigators alike must rely on clinical criteria because there are no pathognomonic laboratory findings

Several diagnostic criteria sets have been proposed

In 1990 ,
the International Study Group established a set of criteria based on the presence of recurrent oral aphthae along with two additional findings from the following list :

- Recurrent genital aphthae
- Cutaneous lesions
- Ocular involvement &
- Positive result on Pathergy testing

Criteria in details

Recurrent aphthous stomatiis , It is basic for diagnosis of Behcet,s disease , as in :

- Ankylosing Spondylitis (no diagnosis without sacroiliitis) ,
- Antiphospholipid Antibody syndrome (no diagnosis without presence of anticardiolipin antibodies in patient,s blood) ,
- Familial Mediterraneam Fever (no diagnosis without attacks of fever) ,
- Till now , no Anti-smith antibodywithout SLE
- No Behcet,s disease without recurrent aphthous stomatitis

Recurrent Oral ulceration

- Minor aphthous, major aphthous , or herpetiform ulceration observed by physician or patient that recurred at least three times in one 12-month period

Plus two of the following criteria :

Recurrent genital ulceration

- Aphthous ulceration or scarring observed by physician or patient

Eye lesions

- Anterior uveitis ,
- Posterior uveitis or
- Cells in vitreous on slit lamp examination OR
- Retinal vasculitis observed by ophthalmologist

Skin lesions

- Erythema nodosum observed by physician or patient ,
- Pseudofolliculitis or
- Papulopstular lesions OR
- Acneiform nodules observed by physician in postadolescent patients not on corticosteroid treatment

Positive Result on Pathergy Testing

- Read by physician at 24 to 48 hours

These criteria were found to have a sensitivity of 91% & Specificity of 96%

Guidelines for treatment of Behcet's Disease

Garton R A , et al , Behcet,s disease , Kelley,s textbook of rheumatology , seventh edition , chapter 86 , 1396 – 1401 , 2005

Therapeutic options should be based on the degree of involvement

Mucocutaneous disease :

- Topical , intralesional , or aerosolized GCs
- Local anaesthetics
- Topical tacrolimus
- Colchicine (0.6 to 1.8 mg / day)
- Dapsone (50 to 100 mg / day)

- Combinations of these agents

Patients who fail to respond to these previous conservative therapy or :

Severe Mucocutaneous Disease

- Thalidomide (100 mg / day) ; relatively safe & effective

If no response :

- Methotrexate (7.5 to 20 mg / week) ; plus
- Prednsone (low-dose)

If no enough response

- Interferon alfa (3 to 9 million U / week)

Systemic Disease ;

- Patients with systemic disease such as ocular & cardiovascular abnormalities require immunosuppressive therapy
- Systemic GCs (Prednisone 1mg / kg / day)

Can be used alone or in combination with other immunosuppressive agents :

- Azathioprine
- Chlorambucil
- Cyclophosphamide
- Cyclosporine
- Interferon-alfa

Standard of care for eye disease is prednisone plus Azathioprine

If this combination is not successful , one of the aforementioned immunosuppressive agents may be substituted for the Azathioprine

More recent reports :

- Anti-TNF-alfa agents (Infliximab 3mg / kg , 6 to 8 weeks & Etanercept , 25mg sq, 2 weeks)
- Larger studies looking at the long-term efficacy & safety of these agents are in progress

Calcium Pyrophosphate Dihydrate (CPPD) Crystal Deposition Disease
Pseudogout

Common clinical presentations of CPPD Crystal Deposition Disease

- Asymmetric or incidental finding (e.g. asymptomatic knee fibrocartilage chondrocalcinosis in the elderly)
- Recurrent acute inflammatory monoarticular arthritis (Pseudogout) (e.g. wrist or knee arthritis , sometimes provoked by trauma , concurrent medical or surgical illness , intra-articular hyaluronan) “pseudoseptic arthritis”
- Recurrent acute hemoarthrosis
- Chronic degenerative arthritis (pseudo-osteoarthritis or pseudoneuropathic arthritis)
- Chronic symmetric inflammatory polyarthritis (pseudorheumatoidarthritis)
- Systemic illness (pseudopolymyalgia rheumatic ; fever of unknown origin)
- Destructive arthritis in dialysis-dependent renal failure
- Carpal tunnel syndrome
- Tumoral & pseudotophaceous CPPD crystal deposits
- Central nervous system disease complicating ligamentum flavium or transverse ligament of atlas involvement (cervical canal stenosis , cervical myelopathy , meningismus , foramen magnum syndrome , odontoid fracture)

Proposed Diagnostic Criteria for Calcium Pyrophosphate Dihydrate (CPPD) Crystal Deposition Disease

I – Demonstration of CPPD crystals , obtained by biopsy or aspirated synovial fluid , by definitive means (such as characteristic radiographic diffraction power pattern)

II –

- A - Identification of monoclinic or triclinic crystals showing a weak positive birefringence (or no birefringence by compensated polarized light microscopy
- B - Presence of typical calcifications on radiographs : heavy punctuate & linear calcifications in fibrocartilages , articular (hyaline) cartilages , & joint capsules , especially if bilaterally symmetric

III –

- A - Acute arthritis , especially of knees or other large joints
- B - Chronic arthritis , especially of knees , hip , wrist , carpus , elbow , shoulder & MTP joints , particularly if accompanied by acute exacerbations

Diagnostic Categories :

A- Definite : criteria I or II (A) must be fulfilled
B- Probable : criteria II(A) must be fulfilled
C- Possible : criteria III(A) or III(B) suggests possible underlying CPPD deposition disease

Therapeutics for (CPPD) Crystal Deposition Disease

Terkeltaub R ; Diseases associated with articular deposition of Calcium Pyrophosphate Dihydrate & basic Calcium phosphate Crystals , Kelley,s textbookof rheumatology , seventh edition , chapter 88 ; 1430- 1448 , 2005

- As in gout , therapeutic approaches to patients with CPPD deposition disease involve treatment & prophylaxis of acute arthritic attacks as well as therapy to lessen chronic & anatomically progressive sequelae of crystal deposition .

- Reduced meniscal calcification was reported over a 10-year period in association with administration of oral magnesium to a patient with secondary CPPD deposition disease due to hypomagnesemia. However , there is no specific treatment for idiopathic CPPD deposition disease

Therapeutics for CPPD deposition disease :

- We may classify therapeutic agents used in treatment of CPPD deposition disease according to their response :

Proven benefits

- NSIADs or COX-2 inhibitors
- Intra-articular corticosteroids (GCs)
- Systemic GCs
- Adrenocorticotrophic hormone (ACTH)
- Prophylactic low-dose colchicine

Possible Benefits Already Observed Clinically

- Hydroxychloroquine
- Oral magnesium (for patients with hypomagnesemia)

Theoretical Benefits

- ANK anion channel blockade (Probenicid)
- PC-1 inhibition
- TG2 transglutaminase inhibition
- Phosphocitrate
- Polyphosphate
- Promotion of crystal dissolution by alkaline phosphatase or polyamines

- Episodes of pseudogout generally respond to NSAIDs including COX-2 inhibitors , intra-articular steroids or both , although sometimes more slowly than in gout

- ACTH & systemic GCs , are effective in most cases of acute pseudogout , if not responding to traditional treatment

- The response to colchicines bolus is less consistent than that usually seen in acute gout & IV colchicines is not recommended as treatment for pseudogout ; it can be quite dangerous in elderly patients

- Pseudogout episodes can be diminished in frequency by low-dose daily colchicines prophylaxis

- Pseudorheumatoid CPPD crystal deposition disease is potentially responsive to methotrexate

Basic Calcium Phosphate (BCP) Crystal Arthropathies

Therapeutics For Articular & Periartcular BCP crystal deposition

Proven benefits

- NSAIDs & COX-2 inhibitors
- Local GCs injection
- Local irrigation
- Ultrasonography (US)

Theoretical benefits

- Phosphocitrate
- Modulators of ANK (e.g. probenecid) , PC-1 / NPPI 1, or TG2 transglutaminase

- NSAIDs & local GCs injection are effective treatment options for BCP crystal-associated calcific tendenitis & subacromial bursitis

- BCP crystal-associated inflammation of the rotator cuff & subacromial bursa of he shoulder can be successful treated using needle aspiration , irrigation & steroid injections

- Ultrasound-guided techniques , which promote resorption of rotator cuff & bursal calcification can enhance the success of such approaches

Familial Mediterranean Fever

Diagnostic Criteria for Diagnosis of Familial Mediterranean Fever :

Major Criteria :

- Typical attacks with peritonitis (generalized)
- Typical attacks with pleuritis (unilateral) or pericarditis
- Typical attacks with monoarthritis (hip, knee , ankle)
- Typical attacks with fever alone
- Incomplete abdominal attack

Minor Criteria

- Incomplete attack involving chest pain
- Incomplete attacks involving monoarthritis
- Exertional leg pain
- Favorable response to colchicines

Requirements for diagnosis of FMF are one or more major criteria or two or more minor criteria

Typical attack are defined as recurrent (three or more of the same type) , febrile (38 degree C or higher) & short (lasting between 12 hours & 3 days)

Incomplete attacks are defined as painful & recurrent attacks not fulfilling the criteria for a typical attack

Guideline for treatment of FMF

- Colchicines … up to 2mg / day in divided doses
- If no enough response at 2mg/ day , donot increase , because no more benefits
- If the patient develop drug allergy , no alternative , do desensitization by starting with very smal dose & increase it gradually according to tolerability
- Colchicines during pregnancy (no consensus about its use)
- Colchicines , decrease frequency & severity of attacks , & delay amyloidosis
- If renal transplant is done , do not stop colchicines , because it will protect the transplanted kidney from amyloidosis
- Appendectomy Echocardiography & Chest radiography to avoid misinterpretation & exclude chest & heart diseases or congenital anomalies
- Supportive treatment may be used (NSAIDs) & steroids have no benefit
- Methotrexate may be tried in refractory cases , but no evidence

Fibromyalgia

Criteria for diagnosis of Fibromyalgia

1990 American College of Rheumatology Criteria for Diagnosis of Fibromyalgia

Criteria for Diagnosis of Fibromyalgia Syndrome

At least 3 months of
widespread pain
defined as :
Bilateral
bove & below the waist , including axial skeletal pain
AND
Pain to palpation
with 4-kg pressure
at a minimum of 11 out of 18 predefined tender points

Exclusions

The diagnosis of other diseases does not exclude the diagnosis of Fibromyalgia

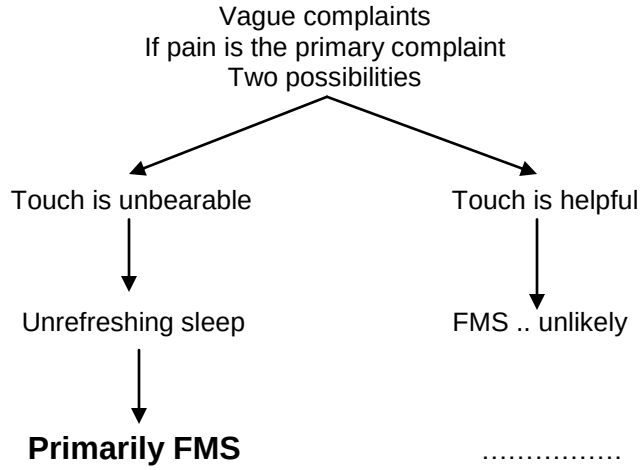
Patients are compared to other rheumatology patients who have chronic painful conditions

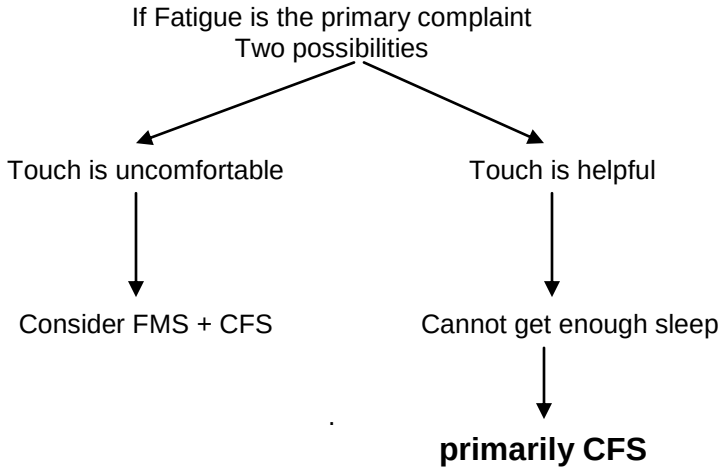
The tender points are located as follows
(each on both sides of the body)

1- The insertion of the suboccipital muscles
2- The anterior aspects of the intertransverse spaces at C5 – C6
3- The midpoint of the upper border of the Trapezius
4- The origin of the supraspinatus , above the scapula spine near the medial border
5- The second rib , just lateral to the costochondral junction
6- Two centimeters distal to the lateral epicondyle
7- The upper outer quadrant of the buttocks in the anterior fold of muscle
8- Just posterior to the greater trochanteric prominence
9- The medial fat pad proximal to the knee joint line

Algorithm for the diagnosis of chronic fatigue syndrome (CFS) & fibromyalgia syndrome (FMS)

Two pathways :





Guidelines for treatment of FMS

Management of FMS :
It is more art tan science at this time, because the pathophysiologic basis of therapy is incompletely understood & few controlled data exist regarding efficacy of several measures employed by practicing physicians

Strategy :

- Firm diagnosis & assurance regarding benign nature of FMS
- Patient education ; avoidance of aggravating factors
- Management of psychologic factors
- Behavioral changes
- Physical exercises & physical fitness
- Physical therapy
- Use of simple analgesics (e.g. acetaminophen = paracetamol) & psychotropic drugs (e.g. amitriptyline & cyclobenzaprine)
- Injection of tender points with local anesthetics
- Referral to psychiatrists : pain clinic

For assessment of management measures :

Effective in Clinical Trials :

- Exercise
- Tricyclics , especially amitripiline
- Cognitive behavioral therapy (It is a process that examines a patient,s way of reacting to experiences & attempts to restructure maladaptive coping habits into effective coping skills

Not effective in clinical trials :

- NSAIDs
- Glucocorticoids

Equivocal or insufficient evidence :

- Opiates (no long term studies)
- Alpha-adrenergic blockade
- Alternative medicine
- Selective serotonin reuptake inhibitors (SSRIs) for mild response in combination with other antidepressants

Likely Harmful :

- Prolonged rest

Gout

Robert L. Wortmann & William N. Kelley , Crystal-induced inflammation , section XIII , Gout & hyperuricemia , Chapter 87 , P: 1402-1429 , Kelley,s textbook of Rheumatology , 2005

The term gout is used to represent a heterogenous group of diseases found exclusively in the human species that include :

1- An elevated serum yrate concentration (hyperuricemia)
2- Recurrent attacks of acute arthritis in which monosodium urate crystals are demonstrable in synovial fluid leukocytes
3- Aggregates of monosodium urate crystals (tophi) deposited chiefly in & around joints, which sometimes lead to deformity & crippling
4- Renal disease involving glomerular , tubular , & interstitial tissues & blood vessels
5- Uric acid nephrolithiasis

These manifestations can occur in various combinations

Criteria for the classification for Acute Gouty arthritis ;

To classify or diagnose your patient as having acute gouty arthritis , he or she should have one of three :

- The presence of characteristic urate crystals in the joint fluid ,
  OR
- A tophus contain uarte crystals by : chemical means or polarized microscopy ,
  OR
- Presence of **6** of the following **12** clinical , laboratory , & radiographic phenomenon ;

1- More than one attack of acute arthritis
2- Maximal inflammation developed within 1 day
3- Attack of monoarticular arthritis
4- Joint redness observed
5- First metatarsophalangeal (MTP) joint painful or swollen
6- Unilateral attack involving first MTP
7- Unilateral attack involving tarsal joint

8- Suspected tophus
9- Hyperuricemia
10- Asymmetric swelling within a joint (radiograph)
11- Subcortical cysts without erosions (radiographs)
12- Negative culture of joint fluid for micro-organisms during attack of joint inflammation

For treatment of gouty arthritis , you have to determine your aims , then each aim has its measure to approach :

The therapeutic aims in gout are as follows :

1- To terminate the acute attack as promptly & generally as possible
2- To prevent recurrence of acute gouty arthritis
3- To prevent or reverse complications of the disease resulting from deposition of sodium urate or uric acid crystals in joints , kidneys or other sites
4- To prevent or reverse associated features of the illness that are deleterious , such as obesity , hypertriglyceridemia & hypertension

Acute Gouty Arthritis

To terminate
Use one of three
1- Colchicine
2- NSAIDs
3- GCs

The time of initiation of therapy is more important then the choice of drug . With any of these agent s , the sooner the drug is started , the more rapidly a complete response will be attained

Colchicine is preferred for patients in whom are the diagnosis of gout is not confirmed

NSAIDs are preferred when the diagnosis is secure

If the patient can not take medication by mouth or has active peptic ulcer disease , the choice is among
- IV colchicines
- Intra-articular GCs , or
- Parenteral GCs

Local application of ice packs may help control the pain of an acute attack

Antihyperuricemic agents , should not be changed (either started or stopped) during an acute attack . Just as sudden fluctuation in serum urate levels may tend to

precipitate an acute attack , an inflammation reaction already in progress may be made substantially worse by a major change in the serum urate concentration

Guidelines for use of Colchicine in Gouty arthropathy

- It can be administered by oral or intravenous routs
- Orally : a dose of 0.5 or 0.6 mg is taken hourly until one of three things occurs :
  1- Joint symptoms ease
  2- Nausea , vomiting or diarrhea develops , or
  3- The patient has taken a maximum of 10 doses

If 10 doses are taken without benefit , the clinician should question the accuracy of the diagnosis .

In most patients , the side effects precede or coincide with improvement in joint symptoms

The use of IV colchicines is associated with some risk
Although this form of therapy (IV) is effective , the reports of severe toxicity & death caused by inappropriate use of the medication are too plentiful .

Control of Hyperuricemia

Elimination of hyperuricemia with antihyperuricemic agents can prevent as well as reverse urate deposition
Allopurinol is presently the only Xanthine oxidase inhibitor approved for use :

Guidelines for use of or Indications of Allopurinol

Hyperuricemia associated with increased uric acid production

- Urinary uric acid excretion of 1000mg or more in 24 hours
- Uric acid nephropathy
- Nephrolithiasis
- Pophylaxis before cytolytic therapy
- Hyperuricemia associated with HPRT deficiency or PRPP synthetase overactivity

Intolerance or reduced efficacy of space uricosuric agents

- Gout with renal insufficiency (Glomerular filtration Rate < 60 ml/min)
- Allergy to uricosurics

Hemochromatosis

An arthropathy can be associated with hemochromatosis in 50% of cases & often is the presenting complaint . Males usually are afflicted , but arthritis can occur in females before menopause . Misdiagnosis or lengthy delays before diagnosis unfortunately are the rule

In most cases the arthropathy accompanies hemochromatosis with clinical & histologic evidence of liver involvement & elevated serum iron & transferring levels

Clinical algorithm for Diagnosis of Hemochromatosis

If you suspect a case of hemochromtosis
With negative Family history

Ask for
Fasting transferritin saturation
(For screening)

If it is normal
(< 50% female & < 60% male)
No further evaluation

But if is elevated

Ask for :
HFE testing

Kawasaki's Disease

It is an acute febrile illness associated with systemic vasculitis that primary affects infants & young children

Criterion For A Diagnosis of Kawasaki's Disease :

Criterion	**Occurrence (%)**
1-Fever lasting 5 days or more	100 %
2-Changes of lips & oral cavity A- Dry , red , vertically fissured lips B- Strawberry tongue C- Diffuse erythema of mucous membranes	90%
3-Bilateral non-suppurative , bulbar conjunctivitis	85%
4-Polymorphous rash (primary on trunk)	80%
5-Changes of peripheral extremities A- Erythema of palms & soles B- Indurative edema of hands & feet C- Desqumation from digital tips	70%
6-acute non-purulent enlargement of cervical lymph node to more than 1.5 cm in diameter	70%

- Five criteria are required for diagnosis OR
- Four criteria plus coronary aneurysms on Echocariography
- For criteria 2 & 5 , any one of the three findings will suffice

Low Back Pain

Differential Diagnosis of Low Back Pain (LBP)

- Idiopathic LBP (80%)
- Disc herniation
- Degenerative disc disease
- Intervertebral disk annular tears
- Spinal stenosis
- Fracture
- Spondylolisthesis
- Spondyloarthropathies
- Infection
- Malignancy
- Cauda equina syndrome
- Renal disease
- Vascular disease
- Psychosocial issues

Red flags

An important points in the history that indicate a possible serious underlying conditions as a source for LBP

Presence of any of these symptoms is an indication for obtaining special diagnostic studies

---

Red flags for Spinal Fracture

- History of Significant trauma
- Moving-vehicle accident
- Fall OR Direct blow in a young person
- Minor fall or heavy lift in a potentially osteoporotic person
- Prolonged use of steroids
- Age > 70 years

Red flags for Cancer or Infection :

- History of Cancer
- Unexplained weight loss
- Immunosuppression
- Intravenous drug use
- History of urinary infection
- Pain increased by rest
- Fever
- Age > 50 years

Red Flags for Cauda Equina Syndrome

- Bladder dysfunction
- Urinary retention
- Overflow incontinence
- Bowel dysfunction
- Loss of anal sphincter tone
- Fecal incontinence
- Saddle anaesthesia
- Global or progressive motor weakness

Guide for examination of Low Back Disorders

Twenty –one test items to be observed during a logical sequence of patient positioning They require 12 to 13 minutes to complete

The tests were classified according to patient,s position , some of them well done in standing , then ask your patient to sit down , then ask him to lay down in supine position & lastly lay down in prone .

Tests in Standing Position

- Single trunk flexion
- Single trunk extension
- Repeated trunk flexion
- Repeated trunk extension
- Trunk twist
- Head compression

During performing the tests , you have to observe posture , deformities , attitude , face expressions , smoothening of the motion & difficulties .

Tests in Seated Position

- Seated Straight Leg Raising (SLR) – left
- Seated Straight Leg Raising – right

Tests in Supine Position

- Single Williams knee pull
- Repeated Williams knee pull
- Supine SLR – right
- Supine SLR – left
- Bilateral active SLR

Tests in Prone Position

- Skin tenderness
- Single partial push-up
- Repeated partial push – up
- Back tenderness
- Instability test
- Femoral stretch-right
- Femoral stretch-left

Test for Consistency

- Incongruence (between sitting & supine SLR)

Abbreviated Neurologic Examination

Strength

- Dorsiflexion of Ankle ….. L4
- Dorsiflexion of great Toe ….. L5
- Ankle reflexes ….. S1

Light Touch in the foot

- Medial ….. L4
- Dorsal ….. L5
- Lateral ……S1

Straight Leg Raise

Reflexes

- Knee jerk
- Ankle reflex

Special Studies & Diagnostic Considerations

Special Studies : Tests for Physiologic Dysfunction

1-Electromyography (EMG)

- Needle EMG & H-reflex : It is useful for patients with leg symptoms > 4 weeks
- It is not recommended if radiculopathy is present
- Surface EMG & F-wave : It is not recommended
- Somatosensory evoked potentials (SEP) : It is useful in spinal stenosis & spinal cord myelopathy

2-Bone scan

- It is recommended if Red flags are present

3-Thermography

- It is not recommended

Special Studies : Tests to provide Anatomic Definition

Plain Radiographs

- Not recommended unless a red flag is present
- Recommended for patients with red flags for fracture
- Recommended in combination with CBC & ESR for patients with red flags for tumor or infection
- Other imaging indicated if radiographs are negative in the presence of red flags
- Oblique view : not recommended

Indications for Imaging Studies

Red Flags for Cauda Equina Syndrome :

- Prompt CT , MRI , myelography , OR CT-myelography & surgical consultation

Red Flags for Tumor , Infection OR Fracture :

- Prompt CT , MRI , myelography , OR CT-myelography & surgical consultation

Symptoms for < 1 month without red flags :

- Spinal Imaging Tests not recommended

Symptoms for > 1 month

- Imaging test acceptable when surgery is being considered

Prior Back Surgery

- MRI with contrast imaging test of choice

CT-myelography & Myelography

- Invasive , indicated only in special situations for preoperative planning

Sometimes Radiographs are indicated early for evaluation of LBP

Nine Indications for radiographs on initial evaluation for LBP :

- Age > 50 years
- Fever
- Ankylosing spondylitis
- History of malignancy
- Weight loss
- Trauma
- Motor deficit
- Litigation or compensation
- Steroids
- Drug abuse

Indications for early CT scan , MRI , or Bone scan :

- Very high ESR
- Sphincter disturbances
- Refractory cases to traditional therapy (e.g. NSAIDs)
- Night agonizing pain even with complete rest
- History of malignancies ▪▪▪▪ Others

Guidelines for management of Acute Low Back Pain

AHCPR guidelines (Agency for Health Care Policy &Research guidelines) (USA)

1-Patient Information

Patient education
Back school

- Booklets effective
- May be effective for worksite specific education
- Nonoccupational setting : efficacy not shown

2-Symptoms control : medications

Acetaminophen :

- Safe & acceptable

NSAIDs

- Acceptable but hve potential side effects

Muscle relaxants

- Option , not for more effective than NSAIDs

Opioid analgesics

- Option ; side effects & dependence a concern

Phenylbutazone

- Not recommended

Oral steroids

- Not recommended

Antidepressants medication

- Not recommended

Colchicines

- Not recommended

Physical Treatments

Special Manipulation

Acute Low Back Pain without radiculopathy

- Effective

Low Back Pain > 1 month

- Inconclusive

Radiculopathy

- Inconclusive

Physical agents & Modalities

Heat

- Option : self application of heat or cold

Massage

- Insufficiency proven

Ultrasound :

- Insufficiency proven

Cutaneous Laser treatment :

- Insufficiency proven

Electrical stimulation (not TENS) :

- Insufficiency proven

TENS

- Not recommended

Shoe insoles

- Option

Shoe lifts

- Not recommended for leg length inequality < 2 cm

Lumbar corsets & Back belts

- Not proven beneficial for treatment
- May reduce time lost from workin individuals required to do frequent lifting

Traction :

- Not recommended

Biofeedback

- Not recommended

Injection treatments

Trigger point

- Not recommendedligamentous
- * not recommended

Facet joint

- Not recmmoended

Epidural

- No evidence for back pain without radiculopathy
- Option for short-term relief of radicular pain

Acupuncture

- Not recommended

Mixed Connective Tissue Disease (MCTD)

Criteria for diagnosis of Mixed Connective Tissue Disease

The central premise of MCTD is that of an overlap syndrome embracing features of

- SLE
- Scleroderma
- Polymyositis / Dermatomyositis

These overlap features of MCTD seldom occur concurrently , it usually takes several years before enough overlapping features have appeared to be confident that MCTD is the most appropriate diagnosis

The most common clinical associations with U1 RNP antibodies in the early phase of the disease are :

- Hand edema
- Arthritis
- Raynaud,s phenomenon
- Inflammatory muscle disease
- Sclerodctyly

There are 4 diagnostic criteria sets that have been used for defining MCTD patients

A comparative study indicated that two criteria sets , those of Alarcon-Segovia & Khan , had the best sensitivity & specificity (62.5 & 86.5% respectively)

The sensitivity could be improved to 81.3% if the term Myalgia was substituted for Myositis

Alarcon-Segovia,s Criteria

A-Srologic Criteria :

- Anti-RNP at hemoagglutination

B-clinical Criteria :

- Swollen hands
- Synovitis
- Myositis (biologically proven)
- Raynaud,s phenomenon

- Acrosclerosis

MCTD present if :
Criterion A is accompanied by 3 or more clinical criteria , one of which must include synovitis or myositis

Kahn,s Criteria

A-Serologic Criteria

- High titer anti-RNP , corresponding titer of > 1:1600 to a speckled antinuclear antibodies (ANA) of > 1:1200 titer

B-Clinicl criteria :

- Swollen fingers
- Synovitis
- Myositis
- Raynaud,s phenomenon

MCTD present if :
Criterion A is accompanied by Raynaud,s phenomenon & two of the three remaining clinical criteria

Guidelines for managing MCTD

Fatigue , Arthralgia , Myalgia

- NSAIDs
- Antimalarials
- Low dose prednisone (less than 10 mg / day)

Arthritis

- NSAIDs
- Antimalarials
- Gold
- Methotrexate
- ? TNF inhibition

Pleurisy

- Indomethacin
- Short course of prednisone (about 20mg/day)

Aseptic meningitis

- Discontinue NSAIDs
- Short course of high dose of prednisone (about 60mg/day)

Myositis

- Acute onset/severe : prednisone , 60 to 100 mg / day
- Chronic / low-grade : prednisone , 10 to 30 mg/day
- Consider methotrexate & IVIG

Membranous glomerulonephropathy

- Mile : No treatment required
- Progressive proteinuria : trial of angiotensin-converting enzyme inhibitor ; trial of low dose aspirin combined with dipyridamole
- Severe : trial of prednisone (15 to 60 mg/day) plus monthly pulse cyclophosphamide (CYC) or daily chlorambucil

Nephrotic Syndrome

- Steroids seldom effective
- Low-dose aspirin combined with dipyridamole to prevent thrombotic complications
- Trial of prednisone (15 to 60 mg/day) plus monthly pulse CYC or daily chlorambucil
- May require dialysis / transplantation

Rynaud,s phenomenon

- Keep warm
- Avoid finger trauma
- Stop smoking
- Nifedipine as tolerated
- Pentoxifyline in severe cases with ischemic eschars

Acute –onset digital gangrene

- Intra-arterial Prostacyclin
- Local nitroglycerine ointment
- Consider endothelin receptor antagonist such as bosentan (Tracleer)

Myocarditis

- Trial of steroids& CYC
- Avoid digoxin

Incomplete heart block

- Avoid chloroquine

Asymptomatic pulmonary hypertension

- Trial of steroids & CYC
- Low dose aspirin & angiotensin-converting enzyme inhibitors
- Consider Endothelin receptor antagonist (oral bosentan)

Symptomatic pulmonary hypertension

- Intravenous Prostacyclin
- Angiotensin-concveting enzyme inhibitors
- Anticoagulation
- Oral bosentan
- Sildenafil trial
- Heart/lung transplantation

Vascular headache

- Trial of propanolol OR
- Alternate day aspirin (350mg)
- Symptomtic use of sumatripin

Dysphagia

- Mild : no treatment
- With reflux : proton pump inhibitor ; consider Nissen fundoplication
- Severe : calcium channel antagonist , alone or in combination with an anticholinergic agent

Intestinal dysmobility

- Prokinetic agentssuch as metochlopramide , domperidone , octretide & erythromycin
- Small bowel bacterial overgrowth : tetracycline , erythromycin

Osteoporosis

- Calcium & vitamin supplements
- Estrogen replacement or raloxifen
- Bisphosphonates
- PTH

Heartburn

- Raise head of bed
- Discontinue smoking & avoid caffeine
- H2 ntagonists
- H+ proton blockers
- Metoclopramide trial pump

Trigeminal neuropathy

- None

Muscle Diseases

Inflammatory Diseases of Muscle
Classification of inflammatory diseases of Muscle

Idiopathic inflammatory myopathies

- Polymyositis (PM)
- Dermatomyositis (DM)
- Juvenile (childhood) DM
- Myositis associated with collagen vascular disease
- Myositis associated with malignancy
- Inclusion body myositis

Other forms of inflammatory myopathy

- Myositis associated with Eosinophilia
- Myositis ossificans
- Localized or focal myositis
- Giant-cell myositis

Myopathies caused by infection
Myopathies caused by drugs & toxins

Criteria to Define Polymyositis (PM) & Dermatomyositis (DM)

Proposed by Bohan & Peter

1- Symmetric weakness of limb girdle muscles & anterior neck flexors , progressing over weeks to months , with or without dysphagia or respiratory muscle involvement
2- Skeletal muscle histologic examination showing evidence of necrosis of types I & II muscle fibers , phagocytosis , regeneration with basophilia , large sacrolemmal nuclei & prominent nucleoli , atrophy in a perifascicular distribution , variation in fiber size & an inflammatory exudates
3- Elevation of levels of serum skeletal muscle enzymes (CK , Aldolase , ALT , AST & LDH)
4- Elecromyographic (EMG) tried of short , small polyphasic motor units ; fibrillations , positive waves & insertional irritability & bizarre high-frequency discharges
5- Dermatologic features including a lilac (heliotrope) discoloration of the eyelids with periorbital edema ; a scaly , erythematous dermatitis over the dorsa of the hands , especially over the metacarpophalangeal & proximal interphalangeal joints (Gottron,s sign) & involvement of the knees , elbows , medial maleoli , face , neck & upper torso .

Osteoarthritis

Guidelines for Diagnosis & Management of Osteoarthritis

Carlos J Lozada , Management of Osteoarthritis , chapter 93 , P:1529-1540 , Kelley,s textbook o Rheumatology , seventh edition , 2005

American College of Rheumatology (ACR) Radiologic & Clinical Criteria for Knee & Hip Osteoarthritis (OA)

Knee Osteoarthritis :

Set of Criteria :

- Knee pain

And

- One of the following
- Age > 50 years
- Morning stiffness < 30 minute
- Crepitus

And

- Radiologic osteophytes

Performance :

- Sensitivity = 91 %
- Specificity = 86 %

Hip Osteorthritis :

Set of Criteria

- Hip pain

And

- At least two of the following :
- ESR <20 mm 1st hour
- Radiologic osteophytes
- Radiologic joint space narrowing

Performance :

- Sensitivity = 91%
- specificity = 89%

The management of osteoarthritis (OA) can be divided into :

- Non-pharmacologic interventions
- Pharmacologic interventions
- Surgical options

Pharmacologic interventions can be further subdivided into :

- Symptomatic therapy &
- Potential structure– or disease-modifying therapy

Non-pharmacologic management of OA

Conventional options in the management of OA

- Patient education
- Arthritis self-help courses
- Weight loss
- Temperature modalities
- Exercise
- Orthotics
- Modified activities of daily living

Unconventional Options for OA

- TENS
- Pulsed electromagnetic fields
- Static magnets
- Acupuncture
- Spa therapy
- Yoga

Weight loss :

- Higher body mass index (BMI) is associated with an increased risk of progression of OA of the knee
- Regimes of weight loss & exercise have been associated with improvement in pain & disability inOA of the knee
- Weight loss alone has been associated with a decrease in the odds of developing symptomatic knee OA

Temperature modalities

- Topical application of heat or cold can be helpful adjunct to the therapeutic plan for OA patient
- More effectively in superficial joints

Exercise

- Quadriceps-muscle weakness has been postulated as a risk factor for OA of the knee
- Quadriceps strengthening exercise has been advanced as fundamental to the management of conditions such as chondromalacia patella
- Walking can be beneficial
- Supervised fitness-walking regimens have been shown to improve function in OA of the knee
- Home-based exercise … significantly improve symptoms in those with knee OA

Orthotics & Bracing

- They range from insoles to braces

- *Lateral wedged insoles :* provide substantial relief to those with medial compartment knee OA , particularly those with varus deformity
- Valgus bracing of patients with medial compartment OA has been found to reduce pain & increase levels of activity
- Medial taping of the patella relieving the pain of those with patellofemoral compartment OA by 25%
- For those with calcaneal spurs or foot joint OA in general , appropriate athletic-type footwear should be recommended . A good athletic shoe should provide medial arch support & calcaneal cushioning , as well as good mediolateral stability
- For those with carpometacarpal joint arthritis … use wrist-splint

- *The cane* : It,s use is particularly important in hip OA & sometimes kneeOA
- It has been estimated that cane can provide up to 40% reduction in hip contact forces during ambulation
- The cane should be used in the hand contralateral to the affected hip & should be advanced with the affected limb while walking
- The appropriate cane size is that which results in about a 20-degree flexion of the elbow during use
- A useful approximation is a cane that is equal to the length from the floor to the patient,s greater trochanter

Modifications of Activities of Daily Living

- These interventions can e varied & range from :
- using an elevated toilet seat or shower bench in someone with lower extremity OA to
- using appliances designed to help with the opening of Jars in a patient with hand OA

Guidelines for Symptom-relieving pharmacologic therapies for OA

Topical
Capsaicin
Topical NSAID preparations
Systemic
Acetaminophen
Nonselective NSAIDs
COX-2 inhibitors
Tramadol
Narcotic analgesics
Intra-articular
Corticosteroids
Hyaluronic-acid derivatives

Intra-articular agents :

Corticosteroids

- although there is no role of systemic GCs in OA , local injection of GCs have a long history in the management of OA
- The dose is determined by joint volume … the largest is the knee
- Postinjection flares due to GC crystal synovitis ca occur
- In general : GC injections are believed to be most effective in patients with evidence of inflammation , effusion or both, usually with no more than four GC injections per year are given in a particular joint

Hyaluronic-Acid derivatives

- they are administered intra-articularly
- They require multiple injection courses , with the injections spaced 1 week apart
- Three to 5 injections may be needed according to the type & molecular weight of the derivative
- Although often mentioned as potential structure-modifying agents , these products are presently considered symptom-modifying drugs

Nutriceuticals for OA

- Glucosamine
- Chondroitin sulfate
- Ginger extracts
- Avocado & soy unsaponifiables
- Cat,s claw
- Shark cartilage
- S-Adenosyl-L-methionine (SAMe)

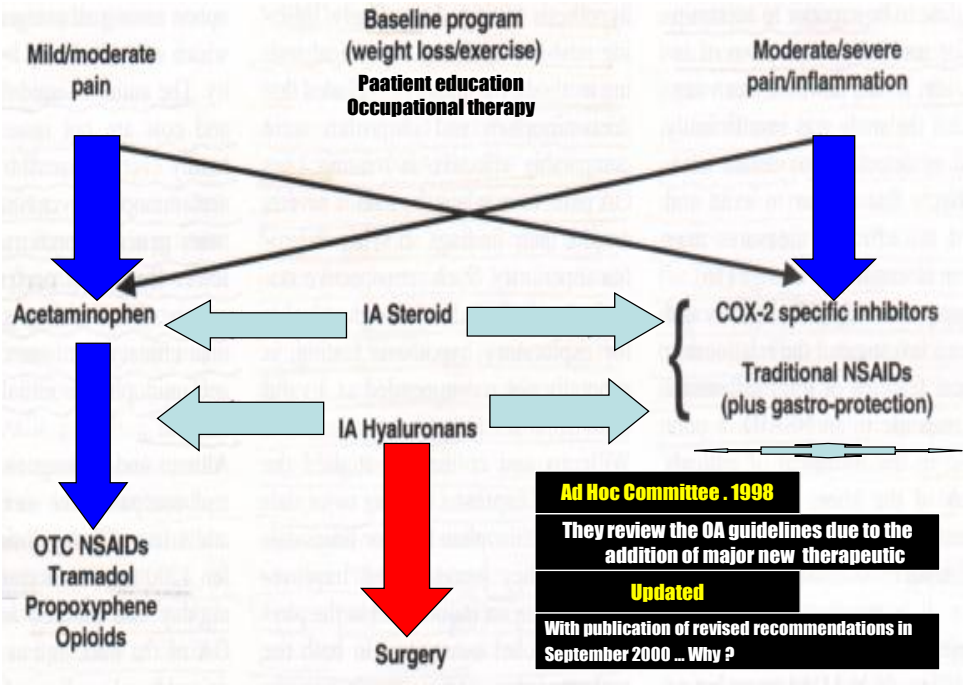
They may be used in treatment of OA with variable benefits … many of trials were reported their success , but the results are beyond the scope of this guideline

Potentially structure- disease Modifying Drugs in OA

- Tetracyclines
- Metalloproteinases or collagenase inhibitors
- Diacerein
- Growth factor & cytokine manipulation (IL-1 receptor antagonist (IL-1Ra) , Transforming growth factor-B (TGF-B1)
- Gene therapy (IL-1Ra , TGF-BII)
- Chondrocyte & stem cell transplants

The term Chondroprotective has been used to describe structure- or disease-modifying agents . This is a misnomer , however , because the goal is to protect the entire joint (not only the cartilage) from the arthritic process

A workshop of the OA research Society (OARS) recommended that the term *Structure- modifying drugs* be used to describe medications that would previously have been classified as chondroprotective
These drugs are intended to prevent , retard , stabilize , or even reverse the development of OA



OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines

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Summary

Purpose: To develop concise, patient-focussed, up to date, evidence-based, expert consensus recommendations for the management of hip and knee osteoarthritis (OA), which are adaptable and designed to assist physicians and allied health care professionals in general and specialist practise throughout the world.

Methods:
Sixteen experts from four medical disciplines (primary care, rheumatology, orthopaedics and evidence-based medicine), two continents and six countries (USA, UK, France, Netherlands, Sweden and Canada) formed the guidelines development team. A systematic review of existing guidelines for the management of hip and knee OA published between 1945 and January 2006 was undertaken using the validated appraisal of guidelines research and evaluation (AGREE) instrument. A core set of management modalities was generated based on the agreement between guidelines. Evidence before 2002 was based on a systematic review conducted by European League Against Rheumatism and evidence after 2002 was updated using MEDLINE, EMBASE, CINAHL, AMED, the Cochrane Library and HTA reports.

The quality of evidence was evaluated, and where possible, effect size (ES), number needed to treat, relative risk or odds ratio and cost per quality-adjusted life years gained were estimated. Consensus recommendations were produced following a Delphi exercise and the strength of recommendation (SOR) for propositions relating to each modality was determined using a visual analogue scale.

Results:
Twenty-three treatment guidelines for the management of hip and knee OA were identified from the literature search, including six opinion-based, five evidence-based and 12 based on both expert opinion and research evidence.

Twenty out of 51 treatment modalities addressed by these guidelines were universally recommended.

ES for pain relief varied from treatment to treatment.

- Overall there was no statistically significant difference between non-pharmacological therapies [0.25, 95% confidence interval (CI) 0.16, 0.34] and pharmacological therapies (ES ¼ 0.39, 95% CI 0.31, 0.47).

- Following feedback from Osteoarthritis Research International members on the draft guidelines and six Delphi rounds consensus was reached on 25 carefully worded recommendations.

- Optimal management of patients with OA hip or knee requires a combination of non-pharmacological and pharmacological modalities of therapy.

- Recommendations cover the use of 12 non-pharmacological modalities: education and self-management, regular telephone contact, referral to a physical therapist, aerobic, muscle strengthening and water-based exercises, weight reduction, walking aids, knee braces, footwear and insoles, thermal modalities, transcutaneous electrical nerve stimulation and acupuncture.

Eight recommendations cover pharmacological modalities of treatment including

1- acetaminophen,
2- cyclooxygenase-2 (COX-2) non-selective and selective oral non-steroidal anti-inflammatory drugs (NSAIDs),
3- topical NSAIDs and capsaicin,
4- intra-articular injections of corticosteroids and hyaluronates,
5- glucosamine and/or chondroitin sulphate for symptom relief;
6- glucosamine sulphate, chondroitin sulphate and
7- diacerein for possible structure-modifying effects and
8- the use of opioid analgesics for the treatment of refractory pain.

- There are recommendations covering five surgical modalities: total joint replacements, unicompartmental knee replacement, osteotomy and joint preserving surgical procedures; joint lavage and arthroscopic debridement in knee OA, and joint fusion as a salvage procedure when joint replacement had failed. Strengths of recommendation and 95% CIs are provided.

Conclusion :
Twenty-five carefully worded recommendations have been generated based on a critical appraisal of existing guidelines, a systematic review of research evidence and the consensus opinions of an international, multidisciplinary group of experts.

The recommendations may be adapted for use in different countries or regions according to the availability of treatment modalities and SOR for each modality of therapy.

American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee

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Objective.
To update the American College of Rheumatology (ACR) 2000 recommendations for hip and knee osteoarthritis (OA) and develop new recommendations for hand OA.

Methods.
A list of pharmacologic and nonpharmacologic modalities commonly used to manage knee, hip, and hand OA as well as clinical scenarios representing patients with symptomatic hand, hip, and knee OA were generated. Systematic evidence-based literature reviews were conducted by a working group at the Institute of Population Health, University of Ottawa, and updated by ACR staff to include additions to bibliographic databases through December 31, 2010. The Grading of Recommendations

Assessment, Development and Evaluation approach, a formal process to rate scientific evidence and to develop recommendations that are as evidence based as possible, was used by a Technical Expert Panel comprised of various stakeholders to formulate the recommendations for the use of nonpharmacologic and pharmacologic modalities for OA of the hand, hip, and knee.

Results.

Both "strong" and "conditional" recommendations were made for OA management. Modalities conditionally recommended for the management of hand OA include instruction in joint protection techniques, provision of assistive devices, use of thermal modalities and trapeziometacarpal joint splints, and use of oral and topical nonsteroidal antiinflammatory drugs (NSAIDs), tramadol, and topical capsaicin. Nonpharmacologic modalities strongly recommended for the management of knee OA were aerobic, aquatic, and/or resistance exercises as well as weight loss for overweight patients. Nonpharmacologic modalities conditionally recommended for knee OA included medial wedge insoles for valgus knee OA, subtalar strapped lateral insoles for varus knee OA, medially directed patellar taping, manual therapy, walking aids, thermal agents, tai chi, selfmanagement programs, and psychosocial interventions. Pharmacologic modalities conditionally recommended for the initial management of patients with knee OA included acetaminophen, oral and topical NSAIDs, tramadol, and intraarticular corticosteroid injections; intraarticular hyaluronate injections, duloxetine, and opioids were conditionally recommended in patients who had an inadequate response to initial therapy. Opioid analgesics were strongly recommended in patients who were either not willing to undergo or had contraindications for total joint arthroplasty after having failed medical therapy. Recommendations for hip OA were similar to those for the management of knee OA.

Conclusion.

These recommendations are based on the consensus judgment of clinical experts from a wide range of disciplines, informed by available evidence, balancing the benefits and harms of both nonpharmacologic and pharmacologic modalities, and incorporating their preferences and values. It is hoped that these recommendations will be utilized by health care providers involved in the management of patients with OA.

Nonpharmacologic recommendations for the management of hand OA*

We conditionally recommend that health professionals should do the following:

- Evaluate the ability to perform activities of daily living (ADLs)
- Instruct in joint protection techniques
- Provide assistive devices, as needed, to help patients perform ADLs
- Instruct in use of thermal modalities
- Provide splints for patients with trapeziometacarpal joint OA

No strong recommendations were made for the nonpharmacologic management of hand osteoarthritis (OA).

- The evidence supporting these interventions demonstrated only a small to moderate effect size (see supplementary bibliography for hand OA in Supplementary

Appendix B, available in the online version of this article at http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)2151-4658).

Pharmacologic recommendations for the initial management of hand OA*

We conditionally recommend that health professionals should use one or more of the following:

- Topical capsaicin
- Topical NSAIDs, including trolamine salicylate
- Oral NSAIDs, including COX-2 selective inhibitors
- Tramadol

We conditionally recommend that health professionals should not use the following:

- Intraarticular therapies
- Opioid analgesics

We conditionally recommend that

- persons age _75 years should use topical rather than oral NSAIDs.
- In persons age _75 years, the TEP expressed no preference for using topical rather than oral NSAIDs.

No strong recommendations were made for the pharmacologic management of hand osteoarthritis (OA).

- For patients who have an inadequate response to initial pharmacologic management, please see the Results for alternative strategies. NSAIDs _ nonsteroidal antiinflammatory drugs; COX-2 _ cyclooxygenase 2;

Nonpharmacologic recommendations for the management of knee OA

We strongly recommend that patients with knee OA should do the following :

- Participate in cardiovascular (aerobic) and/or resistance land-based exercise
- Participate in aquatic exercise
- Lose weight (for persons who are overweight)

We conditionally recommend that patients with knee OA should do the following :

- Participate in self-management programs
- Receive manual therapy in combination with supervised exercise
- Receive psychosocial interventions
- Use medially directed patellar taping
- Wear medially wedged insoles if they have lateral compartment OA
- Wear laterally wedged subtalar strapped insoles if they have medial compartment OA
- Be instructed in the use of thermal agents
- Receive walking aids, as needed
- Participate in tai chi programs
- Be treated with traditional Chinese acupuncture*
- Be instructed in the use of transcutaneous electrical stimulation*

We have no recommendations regarding the following :

- Participation in balance exercises, either alone or in
- combination with strengthening exercises
- Wearing laterally wedged insoles
- Receiving manual therapy alone
- Wearing knee braces
- Using laterally directed patellar taping

These modalities are conditionally recommended only when

- the patient with knee osteoarthritis (OA) has chronic moderate to severe pain and is a candidate for total knee arthroplasty but either is unwilling to undergo the procedure, has comorbid medical conditions,

or

- is taking concomitant medications that lead to a relative or absolute contraindication to surgery or a decision by the surgeon not to recommend the procedure.

Pharmacologic recommendations for the initial management of knee OA*

We conditionally recommend that patients with knee OA should use one of the following:

- Acetaminophen
- Oral NSAIDs
- Topical NSAIDs
- Tramadol
- Intraarticular corticosteroid injections

We conditionally recommend that patients with knee OA should not use the following:

- Chondroitin sulphate
-
- Glucosamine
- Topical capsaicin

We have no recommendations regarding the use of

- intraarticular hyaluronates,
- duloxetine, and
- opioid analgesics

No strong recommendations were made for the initial pharmacologic management of knee osteoarthritis (OA).

- For patients who have an inadequate response to initial pharmacologic management, please see the Results for alternative strategies. NSAIDs _ nonsteroidal antiinflammatory drugs.

Nonpharmacologic recommendations for the management of hip osteoarthritis (OA)

We strongly recommend that patients with hip OA should do the following:

- Participate in cardiovascular and/or resistance landbased exercise
- Participate in aquatic exercise
- Lose weight (for persons who are overweight)

We conditionally recommend that patients with hip OA should do the following:

- Participate in self-management programs
- Receive manual therapy in combination with supervised exercise
- Receive psychosocial interventions

- Be instructed in the use of thermal agents
- Receive walking aids, as needed

We have no recommendations regarding the following:

- Participation in balance exercises, either alone or in
- combination with strengthening exercises
- Participation in tai chi
- Receiving manual therapy alone

Pharmacologic recommendations for the initial management of hip OA*

We conditionally recommend that patients with hip OA should use one of the following:

- Acetaminophen
- Oral NSAIDs
- Tramadol
- Intraarticular corticosteroid injections

We conditionally recommend that patients with hip OA should not use the following:

- Chondroitin sulphate
- Glucosamine

We have no recommendation regarding the use of the following:

- Topical NSAIDs
- Intraarticular hyaluronate injections
- Duloxetine
- Opioid analgesics

No strong recommendations were made for the initial pharmacologic management of hip osteoarthritis (OA).

- For patients who have an inadequate response to initial pharmacologic management, please see the Results for alternative strategies. NSAIDs _ nonsteroidal antiinflammatory drugs.

Osteoporosis

Review of Guidelines For Testing & Treatment of Osteoporosis

Piet P.M.M. Geusens , MD, PhD . Current Osteoporosis Reports (2003) Netherland , 1 : 56-65 . Current Science Inc, ISSN 1544-1873 .

Our knowledge on diagnosis & treatment of osteoporosis (OP) has steadily increased during the past decade . Several guidelines on treatment of OP are now available .

Although there is heterogeneity in these recommendations , there are several common suggestions found .

Case finding is advocated in all ; however , it is generally acknowledged that further research is necessary to evaluate the effectiveness of case –finding strategies.

For Diagnosis :

Dual – energy X ray absorptiometry (DEXA) is considered the gold standard for diagnosis of OP . The use of T-score is different for diagnostic purposes & for the treatment decisions .

Other bone measurement techniques are proposed at risk evaluation or as alternatives when DEXA is not available
Bone markers are considered for evaluation in clinical practice

Case Finding for Osteoporosis & Fractures

Risk Factors :

I - Family History

- Degree of family relation , first degree , mother , grand-mother &
- the type of fracture that has occurred (unspecified , osteoporotic fracture , fragility fracture , specific fracture such as hip , vertebra)

II - Estrogen deficiency

- Female gender
- Estrogen deficiency

- Low endogenous estrogen levels
- Early menopause
- Late menarche
- Prolonged premenopausal amenorrhea & not on hormonal therapy (HRT)

III - The description of Ethnicity

- Ethnicity in general
- White race
- Caucasian
- Asian

IV - History of fractures

- Prior fracture after 40 years of age
- Prior vertebral fracture
- Body weight
- Low body weight
- Low body mass index
- Weight loss

V - Lifestyle risk factors

- Smoking
- Alcoholism
- Excessive caffeine intake
- Low Calcium intake
- Low vitamin D intake

VI - Nonskeletal risk factor for fractures

- Factors related to muscle strength include physical activity
- Current & previous exercise
- Immobilization
- Disturbed balance
- Low gait speed

VII - History of falls

- Propensity to fall
- Impaired vision
- Impaired hearing
- Poor health
- Frailty
- Environmental hazards
- Neurologic diseases
- Arthritis
- Being institutionalized
- Direction of falls

- Bone geometry
- Physical signs of vertebral osteoporosis
- Loss of height
- Back pain
- Suspected vertebral fracture

VIII - Glucocorticoid use

IX - Other diseases

- (e.g. RA)

X - Low Bone mineral density (BMD)

XI - Osteopenia in radiographs

XII - Drugs

- (anticoagulants & anticonvulsants)

All guideline recommend a case finding strategy in which patients are identified by the presence of one or more risk factors

Indications for Bone Densitometry

- All postmenopausal women < 65 years who have one or more additional risk factors for OP , besides menopause
- All women > 65 years regardless of additional risk factors
- Documenting reduced bone density in a patient with a vertebral abnormality or osteopenia on a radiograph

- Estrogen –deficient women at risk for low bone density , constituting use of estrogen or an alternative therapy, if bone density would facilitate the decision
- Women who have been on estrogen replacement therapy for prolonged periods or to monitor the efficacy of a therapeutic intervention or interventions for OP
- Diagnosing low bone mass in glucocorticoid-treated individuals
- Documenting low bone density in patients with asymptomatic primary or secondary hyperparathyroidism
- Unexplained fractures
- Anticoagulants & Barbiturates for long time

FRAX
The WHO Fracture Assessment Tool

MARCH 18, 2008

The National Osteoporosis Foundation has released a 2008 update to the NOF guidelines last published in 1999. The guidelines, which are evidence based whenever possible, provide recommendations for screening, counseling and treatment of osteoporosis. This update was prompted by the publication of the FRAX, a new fracture risk assessment tool.

FRAX

The World Health Organization has developed this new fracture risk assessment tool to identify individuals at high risk of osteoporotic fracture The current standard, which bases treatment decisions largely on bone mineral density measurement, has proven to be specific, but not sensitive, for the identification of patients at high risk of fracture. Because nearly 50% of postmenopausal women in the community over the age of 50 years who suffer an osteoporotic fracture do not have osteoporosis defined by a BMD test1,2, and because of the limited availability of BMD in many countries, clinical risk factors were added to BMD to identify patients at high risk for osteoporotic fractures3.

A task force from the WHO evaluated the *clinical* risk factors that predict increased risk of *fracture* in nearly all of the 12 population cohorts evaluated worldwide. These are:

- Age
- Sex
- Prior fragility fracture after age 50
- History of corticosteroid use (5 mg or more for three months or more)
- Parental history of hip fracture
- Rheumatoid arthritis

- Secondary osteoporosis (e.g., type 1 diabetes, osteogenesis imperfecta in adults, longstanding hyperthyroidism, hypogonadism, premature menopause, chronic malabsorption and chronic liver disease)
- Current smoker
- Alcohol use of greater than 2 units daily (a unit is one medium glass of wine or a glass of beer)
- Body Mass Index

FRAX integrates the future osteoporotic fracture risk associated with clinical risk factors with that associated with femoral neck BMD. BMD of the femoral neck (although less data is available, the total hip may also be used in women) tracks in parallel to BMI except at very low BMI, so that BMI may be used when BMD is unavailable. BMI and BMD would not be used in the same individual.

The incident rates of fractures are country specific and provide the clinician the 10 year probability of hip fracture and the 10 year probability of major osteoporotic fracture (clinical vertebral, forearm, hip and shoulder).

FRAX is currenty being validated in additional longitudinal cohort databases. It is anticipated that in the latter half of 2008, the FRAX will be available as a software update for DXA equipment. FRAX is now available to clinicians online at **www.shef.ac.uk/FRAX/** 4,5.

The FRAX provides an estimated fracture risk in a given individual but does not identify the level of fracture risk at which treatment should be started ("intervention threshold"). The intervention threshold decision is based on the willingness of a given country or region to pay for the treatments recommended. For example, in the United Kingdom and Sweden osteoporosis treatment is calculated to be cost-effective for a 4% ten year risk of hip fracture, while in the United States osteoporosis treatment is calculated to be cost-effective with ten year risk of a hip fracture of 3%.

Limitations

The FRAX model is a model in progress. It does not include spinal BMD data or bone turnover markers, as bone marker data is not available from many of the countries that contributed longitudinal cohorts to generate the FRAX.

Also, FRAX does not include data on BMD measured at the peripheral skeletal sites.

Most patients studied for fracture risk were women, and data on ethnic groups in the US are limited.

The FRAX cannot be used in patients who have been treated with osteoporosis medications since the probability of fracture may be overestimated.

Patients being assessed for osteoporotic fracture risk may not be able to make a treatment decision based on a 10 year probability of a fracture, although the one-year probability would be 10% of a ten-year probability.

The-New-NOF-Guidelines

Role of physicians who evaluate, prevent and treat osteoporosis in postmenopausal women and men age 50 and older:

- Counsel on the risk of osteoporosis and related fractures
- Check for secondary causes
- Advise on adequate calcium and vitamin D intake
- Recommend regular weight bearing and muscle strengthening exercise to reduce risk of falls and fractures
- Advise avoidance of tobacco smoking and excessive alcohol intake

BMD testing is advised for:

- Women age 65 and older
- Men age 70 and older
- In younger postmenopausal women and men age 50 and older based on risk factor profile
- Those with a fracture to determine degree of disease severity

Treatment is recommended for:

- Patients with hip or vertebral fracture (clinical or morphometric)
- Patients with osteoporosis as defined by T score <=-2.5
- Postmenopausal women or men age 50 and older with low bone mass (T score -1 to -2.5, osteopenia) at the femoral neck, total hip, or spine and 10 year hip fracture risk probability >3% or a 10 year all major osteoporosis related fracture probability of >20% based on the U.S. adapted WHO absolute fracture risk model

BMD should be monitored two years after initiating therapy and at two-year intervals thereafter.

Bottom Line:

- BMD measurement alone fails to identify a high number of subjects who subsequently develop fractures. The addition of clinical risk factors may indeed be an improvement in risk factor assessment.
-
- While FRAX provides a method to evaluate fracture risk with and without BMD to use for global health, understanding exactly what level of fracture risk is appropriate for therapeutic intervention probably requires additional research.

Indications for Treatment

- Fractures (Fragility fracture , vertebral fracture , nonvertebral fracture , & any fracture … consider the age)
- T-score less than (- 2.5)
- T-score < -1.5 when at least one other risk factor is present

Treatment Options

General Advice

- Cessation of smoking
- Alcohol avoidance
- Decreasing Caffeine intake
- Avoidance of excess sodium
- Maintenance of body weight

Recommendation for prevention of falls

- Physical activity
- Exercise
- Improvement of muscle strength
- Improvement of balance
- Tailored program
- Rehabilitation
- Home Safety

Hip protectors

Adequate Calcium & vitamin D intake

Optimal Calcium Requirements recommended by The National Academy of Sciences (USA)

Infants ;
• Birth – 6 month , daily intake = 400 mg / day • From 6 month to 1 year , daily intake = 600 mg / day
Children :
• From 1 to 8 years , daily intake = 500 to 800 mg / day
Adolescents
• From 9 to 18 years , daily intake = 1300 mg / day • Pregnant & nursing female , daily intake = 1300
Men & women
• From 19 to 50 years , daily intake = 1200 mg / day

Drug Treatment

Antiresorptive agents

HRT

- The Canadian Medical Association (2002) considers HRP a second choice for the treatment of OP , however , an unfacorable risk-benefit ratio as a result of side effects is eported with prolonged use of HRT

Calcitonin

- It is considered in the prevention of vertebral fractures with a high level of evidence (Royal college of physicians 2003 & Hodgson et al 2001)
- It is considered the first choice in the treatment of pain associated with acute vertebral fractures

Raloxifene

- It is considered to be effective in the prevention of vertebral fractures

Bisphosphonates

- They are reported in all guidelines as having a high level of evidence of for the prevention of all fractures including vertebral , nonvetebral & hip fractures
- They are recommended as a first – line drug in the treatment of postmenopausal OP , especially thos with pre-existing vertebral fractures
- Alendronate was shown to decrease the risk by 50% for vertebral & nonvetebral fractures , whereas risedronate was shown to decrease the risk by more than one third for vertebral fractures & 25% for nonvertebral fractures (Cranney et al 2002)

Pamidronate

- It is mentioned in one report & is considered a second –choice bisphosphonate in case of intolerance for oral bisphosphonates , without comments on antifracture effects

Fluoride

- It is not recommended

Where discussed , the effect of intermittent parathyroid hormone (PTH) therapy is considered significant for vertebral , nonvertebral & hip fractures , & it is expected to become a first – line treatment for postmenopausal women with severe OP

European guidance for the diagnosis and management of osteoporosis in postmenopausal women

J. A. Kanis & N. Burlet & C. Cooper & P. D. Delmas &
J.-Y. Reginster & F. Borgstrom & R. Rizzoli &
on behalf of the European Society for Clinical
and Economic Aspects of Osteoporosis
and Osteoarthritis (ESCEO)

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Abstract
Summary
Guidance is provided in a European setting on the assessment and treatment of postmenopausal women with or at risk from osteoporosis.
Introduction The European Foundation for Osteoporosis and Bone disease (subsequently the International Osteoporosis Foundation) published guidelines for the diagnosis and management of osteoporosis in 1997. This manuscript updates these in a European setting.

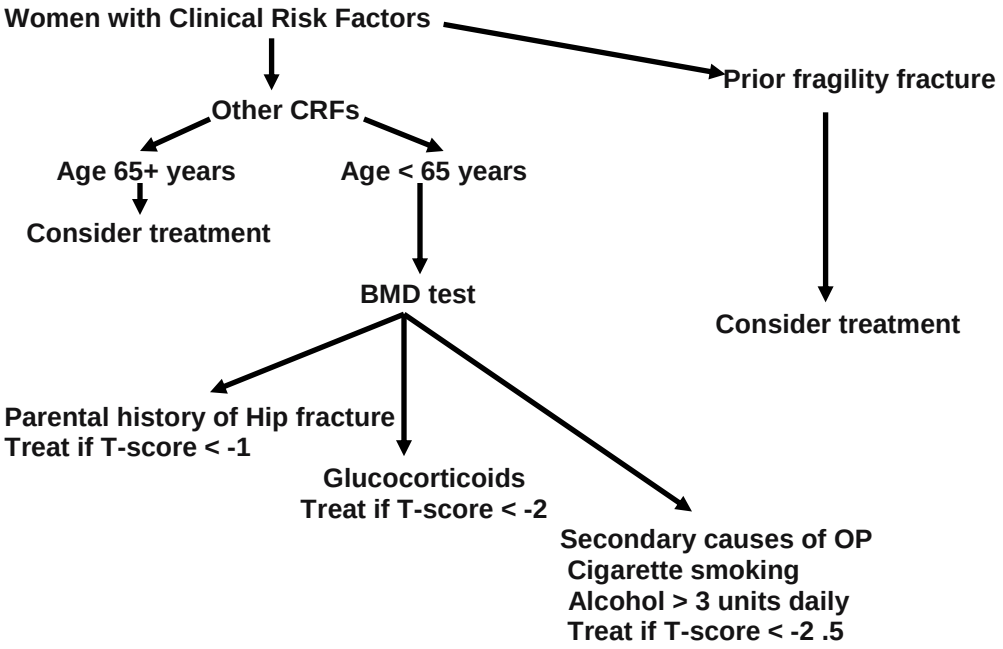
Methods
The following areas are reviewed: the role of bone mineral density measurement for the diagnosis of osteoporosis and assessment of fracture risk; general and pharmacological management of osteoporosis; monitoring of treatment; assessment of fracture risk; case finding strategies; investigation of patients; health economics of treatment.

Results and conclusions
A platform is provided on which specific guidelines can be developed for national use.

Preamble 1997 The European Foundation for Osteoporosis and Bone Disease (subsequently the International Osteoporosis Foundation) published guidelines for the diagnosis and management of osteoporosis [1].
Since then, there have been significant advances in the field of osteoporosis. These include the development of many new techniques for measuring bone mineral, improved methods of assessing fracture risk and new treatments that have been shown to significantly reduce the risk of fractures at vulnerable sites. Against this background, the Scientific

Advisory Board of the European Society for Clinical and Economic Evaluation of Osteoporosis and Osteoarthritis (ESCEO), in collaboration with the International Osteoporosis Foundation, has recognised a need to revise the original guidelines which are detailed below.

The term guideline is supplanted by the term guidance, to avoid any prescriptive connotations since country or region specific guidelines are now widely available. Rather, the guidance can inform the development of new guidelines or the revision of existing guidelines. They are focussed on a European perspective, since there are some differences of approach in other regions of the world.



Management algorithm in postmenopausal women based on an health economic analysis for the UK.

Prevention & Treatment of Glucocorticoid-induced Osteoporosis (GCOP)

Specific guidelines for prevention (from the start of GCs) & treatment (during long-term use of GCs) of GC-induced osteoporosis (GCOP) are included in several general reports & in two specific guidelines

Prevention & treatment if thresholds exceeds

1- Dose threshold : if more than 2.5 or 5 or 7.5 mg /day in different reports
2- Duration threshold : if more than 3 weeks , 3 months or 6 months
3- BMD threshold : if T-score less than -2.5 or -2 or -1.5 in different reports

BMD measurements is recommended in all patients who start GCs

Proposed General measures

- Cessation of smoking
- Avoidance of alcohol
- Appropriate physical activity
- Exercise
- Maximal reduction of GC dose
- Consideration of alternative formulation or routes of administration
- Prescription of alternative immunosuppressive agents

Guidelines advocated

- Adequate Calcium intake
- Ca supplementation
- Unspecified , plain , activated vitamin D supplements
- The proposed dose of plain vitamin D is 800 IU / day , for alfacalcidrol 1.0 ygm/day & for calcitriol 0.5 ygm / day
- Monitoring of serum & urinary Calcium is advocated for patients receiving vitamin D

HRT

- It is recommended in hypogondal women on low to moderate dose of GCs
- In women with menstrual irregularities

Bisphosphonates

- they are recommended for the prevention of GCOP in all patients &
- In patients taking greater than 7.5mg/day
- Or greater than 15mg/day in other reports
- Or in patients > 65 years
- Or T-score less than - 1.0

Polymyalgia Rheumatica (PMR)

The diagnosis of PMR is clinical & depends on eliciting the symptoms & findings noted earlier

Two sets of criteria for the diagnosis have been proposed

Criteria of Chuang & colleagues (1982)

- Age 50 years or older
- Bilateral aching & stiffness for 1 month or more & involving two of the following areas : Neck or Torso , shoulders or proximal regions of the arms & hips or proximal aspects of the thighs
- ESR greater than 40mm/hr
- Exclusion of all other diagnosis except GCA

Criteria of Healey (1984)

- Pain persisting for at least 1 month & involving two of the following areas : Neck , shoulders & pelvic girdle
- Morning stiffness lasting more than 1 hour
- Rapid response to steroids (prednisone) (20 mg / day or less)
- Absence of other diseases capable of causing the musculoskeletal symptoms
- Age more than 50 years
- ESR greater than 40 mm / hr

For each set of criteria , all the findings must be present for PMR to be diagnosed

For diagnosis of Polymyalgia Rheumatica (PMR) without Giant Cell Arteritis (GCA)

If
you suspect PMR without GCA

Give prednisone up to 20 mg / day for 7 days

If there is excellent response

Diagnosis is supported

Continue to monitor for emergence of GCA

If
there is no or poor response after 7 days

Increase prednisone to 30 mg / day for – 7 days

If also no response to prednisone 30 mg / day

Reject diagnosis of PMR & search for alternative diagnosis

1990 Criteria for the classification of Giant Cell (Temporal) Arteritis (Traditional Format)

1-Age at disease onset > 50 years

- Development of symptoms or findings beginning at age 50 or older

2-New headache

- New onset of or new type of localized pain in the head

3-temporal artery abnormality

- Temporal artery tenderness to palpation or decreased pulsation , unrelated to arteriosclerosis of cervical arteries

4-Elevated ESR

- ESR > 50 mm/h by the Westergren method

5-Abnormal artery biopsy

- Biopsy specimen with artery showing vasculitis characterized by a predominance of mononuclear cell infiltration or granulomatous inflammation , usually with multinucleated giant cells

For purposes of classification , a patient with vasculitis is said to have giant cell (temporal) arteritis (GCA) if at least three of these five criteria are present

The presence of any three or more criteria yields :

- Sensitivity of 93.5 % & a
- Specificity of 91.2% .

The diagnosis of GCA should be considered in any patient more than 50 years old who experiences :

- loss of vision ,
- diplopia
- new form of headache
- jaw claudication
- polymyalgia rheumatic (PMR)
- fever of unknown origin
- unexplained constitutional symptoms
- anemia &
- high ESR

GCA can cause many forms of cranial discomfort e.g.

- headache
- scalp tenderness
- jaw claudication , or
- pain in the throat , gums & tongue

The disease should also be considered in any patient older than 50 years who develops new , unexplained (above Neck Pain)

GCA should also be considered in the differential diagnosis of an older patient presenting with a :

- dry cough
- stroke
- arm claudication
- acute C5 radiculopathy

accompanied by other classic symptoms or findings of GCA

Treatment of PMR :

- patients without symptoms or signs or biopsy of evidence of GCA are usually treated with 5 to 20 mg daily doses of prednisone or equivalent
- salicylates & NSAIDs have been used but are less appealing
- minority of patients with isolated PMR fail to respond to prednisone (20 mg / day) after 1 week & may require up to 30 mg of prednisone daily as initil treatment
- failure to respond to prednisone (30mg/day) for 1 week should be prompt a search to for an alternative diagnosis
- The dose should be reduced gradually as soon as symptoms permit
- Some experts have recommended tapering prednisone by 2.5 mg every week until reaching 10mg / day when the decrements should be reduced by 1mg each month
- Flares develop commonly & require raising the prednisone dose to achieve remission before attempting a slower taper
- The minority of patients with PMR will succeed in tapering off prednisone in less than 1 year
- Many require at least 2 years of low-dose prednisone

For GCA

- 40 to 60 mg of prednisone daily in divided doses or equivalent is adequate in nearly all cases
- If no prompt response .. increase the dose
- If visual loss…. Pulse steroid therapy (1gm daily for 3 days)

Reactive Arthritis

Criteria for diagnosis of Reactive Arthritis

- The two entry parameters of the ESSG criteria (inflammatory spinal pain & asymmetric synovitis involving the lower limbs) are also the most important for a correct diagnosis or reactive arthritis (ReA)
- Clinical OR Laboratory evidence of recent infection completes the entry criteria for ReA
- HLA-B27 positivity greatly enhances the accuracy of the diagnosis

Diagnostic Strategy in Reactive Arthritis

- If the patient has inflammatory back pain or oligoarthritis of lower extremity : The patient may have ReA
- If he OR shehas symptoms of preceding acute symptomatic urethritis , cervicitis or enteritis : The probability increases to (30) up to (50%)
- If he OR she showed positive bacterial recognition test : The probability increases to (70) up to (80%)
- If showed positive HLA-B27 : the probability increases up to > 80%

Guidelies for management of SpA & ReA

David Tak Yan Yu & Peng Thim Fan : Spondyloarthropathies , treatment plan , Kelley,s textbook of rheumatology , chapter71, 1142-1155 , 2005

1- Eradicate acute bacterial infection with an antibiotic
2- Use NSAIDs to relieve pain & inflammation
3- Add an opioid if necessary

4- Inject swollen joints & tendons with glucocorticoid
5- For painful sacroiliac joint , inject under computed Tomography (CT) guidance

6- Add DMARDs, if the disease is still active & progressive – Use Salazopyrine if biologics are unavailable

7- Infliximab & Etanercept will lead to rapid & dramatic improvement in the majority of patients with severe disease

The effect of treatment by biologics on the course of these spondyloarthropathies will require many years of follow – up to become clear . The improvement of inflammation observed by MRI is very encouraging .

Relapsing Polychondritis

- It is a rare ,
- long-standing &
- potentially life-threatening disorder characterized by recurrent inflammatory episodes affecting the cartilaginous structures of the external ears , nose , larynx , & tracheobroncheal tree , sometimes lead to their destruction

Systemic manifestations involving

- auricles ,
- eyes ,
- skin ,
- inner ears &
- vessels are frequently associated

Among several sets of clinical diagnostic criteria , the most commonly used is the following :

Empirical Diagnostic Criteria For Relapsing Polychondritis :

Major Criteria :

- Proven inflammatory episodes involving auricular cartilage
- Proven inflammatory episodes involving nasal cartilage
- Proven inflammatory episodes involving laryngotracheal cartilage

Minor Criteria :

- Ocular inflammation (conjunctivitis , Keratitis , Episcleritis , Uveitis)
- Hearing loss
- Vestibular dysfunction
- Seronegative inflammatory arthritis

Diagnosis is made by two major criteria or one major & two minor

Histologic examination of affected cartilage is not required

Guidelines for treatment of Relapsing Polychondritis ;

For Minor cases :

- NSAIDs , Colchicines & / OR Dapsone

Glucocorticoids :

- Cornerstone for a majority of cases

- Initial doses = 0.5 to 1 mg / kg / day
- Methylprednisolone pulses (1 gm / day for 3 days) for frank respiratory flares
- Progressive tapering is frequently limited by the requirement for substantial maintenance doses

Immunosuppression

- It is indicated either initially , insevere respiratory or vasculitic involvement or
- Secondarily to improve disease control & allow steroid tapering

- Methotrexate (0.3 mg / kg / week) is frequently effective & carries no risk of secondary myelodysplasia

Rheumatic Fever (RF)

Acute RF , is
- a delayed ,
- nonsuppurative sequela of a pharyngeal infection with
- a group streptococcus ;

Following the initial streptococcal pharyngitis, there is a latent period of 2 to 3 weeks

The onset of disease is usually characterized by an acute febrile illness , which may manifest itself in one of three classic ways :
1- The patient may present with migratory arthritis predominantly involving the large joints of the body
2- There may be concomitant clinical & laboratory signs of carditis & vasculitis
3- There may be involvement of the CNS , manifesting itself as Sydenham,s chorea

The clinical episodes are self limiting , but damage to the valves may be chronic & progressive , resulting in cardiac decompensation & death

Revised Jones Criteria for Diagnosis of Acute Rheumatic Fever

Major manifestations :
1- Carditis
2- Polyarthritis
3- Chorea
4- Erythema marginatum
5- Subcutaneous nodules

Minor manifestations :
1- Fever
2- Arthralgia
3- Previous rheumatic fever or rheumatic heart disease

Laboratory Findings :

1- Elevated acute phase reactants (CRP & ESR)
2- Prolonged P-R interval rate
3- Supporting evidence of preceding streptococcal infection :

A -Increased ASOT or other streptococcal antibodies
B-Positive throat culture for Group A-hemolytic streptococci
C-Recent scarlet fever

- The clinical presentation of acute RF is quite variable, & the lack of single pathognomonic feature has resulted in the development of the Revised Jones Criteria , which are used to establish a diagnosis of .

- It should be noted that these criteria were established only as guidelines for the diagnosis & were ever intended to be " etched in stone "

- Thus depending on the age , geographical location , ethnic population or some combination of these , emphasis on one criterion for the diagnosis of Acute RF may be more important than others

If RF is suspected by evidence of preceding Group A streptococcal infection , the presence of two major manifestations or one major & two minor manifestations indicates a high probability of acute RF

- Again the modified Jones criteria are only guidelines .
- They are almost difficult to apply confidently when polyarthritis is the single major manifestation .

- Under such circumstances , the diagnosis of acute RF should be made only after excluding causes of polyarthritis such as :RA , Still,s disease , Lyme disease , Viral & septic arthritis , including gonococcal arthritis

Prevention of Rheumatic Fever

Secondary prevention of RF

Prevention of Recurrent Attacks … By

Benzathine Penicillin G
- Dose = 1.200.000 U every 4 weeks
- Intramuscular OR

Penicillin V
- 250 mg daily
- Orally OR

Sulfadiazine ;
- 0.5 gram once daily for patients < 27 kg
- & 1.0 gram once daily for patients > 27 kg

For individuals allergic to Penicillin & Sulfadiazine

Erythromycin :
- 250 mg twice daily
- Orally

In high risk situations administration very 3 weeks is justified & recommended

Duration of Secondary RF Prophylaxis :

Rheumatic Fever with carditis & residual heart disease (persistent valver disease)
- At least 10 years since last episode & t least until age 40 years
- Sometimes life long prophylaxis

RF with carditis but no residual heart disease (no valvular disease)
- 10 years or well into adulthood , whichever is longer

RF without carditis
- 5 years until 21 , whichever is longer

Heart & valvar lesions should be evident with Echocardiographically

Rheumatoid Arthritis

1988 Revised American Rheumatism Association Criteria For Classification of RA

They are seven criteria

1-Morning Stiffness :

- Morning stiffness in & around the joints lasting at least 1 hour before maximal improvement

2-Arthritis of three or more joint areas

- At least three joint areas simultaneously having soft tissue swelling or fluid (not bony overgrowth alone)observed by a physician (the 14 possible joint areas are { right & left } PIP , MCP , wrist , elbow , knee , ankle , & MTP joints)

3-Arhritis of hand joints

- At least one joint area swollen as above in wrist , MCP or PIP joint

4-Symmetric arthritis

- Simultaneous involvement of the same joint areas (as in criterion 2) on both sides of the body (bilateral involvement of the PIP , MCP , or MTP joints is acceptable without absolute symmetry)

5-Rheumatoid nodules :

- Subcutaneous nodules over bony prominences or extensor surfaces , or in juxtra-articular regions , observed by a physician

6-Serum Rheumatoid Factor :

- Demonstration of abnormal amounts of serum rheumatoid factor by any method that has been positive in less than 5% of normal control subjects

7-Radiographic changes :

- Changes typical of RA on PA hand & wrist radiographs , which must include erosions or unequivocal bony decalcification localized to or most marked adjacent to the involved joints (osteoarthritis changes alone do not qualify)

For classification purposes a patient is said to have RA if he or she has satisfied at least four of the seven criteria

Criteria 1 through 4 must be present for at least 6 weeks

Patients with two clinical diagnoses are not excluded

Designation as classic , definite or probable RA is not to be made

ACR/EULAR
2010 Rheumatoid Arthritis Classification Criteria
An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative

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This criteria set has been approved by the American College of Rheumatology (ACR) Board of Directors and the European League Against Rheumatism (EULAR) Executive Committee. This signifies that the criteria set has been quantitatively validated using patient data, and it has undergone validation based on an external data set.
All ACR/EULAR approved criteria sets are expected to undergo intermittent updates.

The American College of Rheumatology is an independent, professional, medical and scientific society which does not guarantee, warrant, or endorse any commercial product or service.

Objective.
The 1987 American College of Rheumatology(ACR; formerly, the American Rheumatism Association) classification criteria for rheumatoid arthritis (RA)

have been criticized for their lack of sensitivity in early disease. This work was undertaken to develop new classification criteria for RA.

Methods.
A joint working group from the ACR and the European League Against Rheumatism devel- oped, in 3 phases, a new approach to classifying RA. The work focused on identifying, among patients newly presenting with undifferentiated inflammatory synovitis, factors that best discriminated between those who were and those who were not at high risk for persistent and/or erosive disease—this being the appropriate current paradigm underlying the disease construct "rheumatoid arthritis."

Results.
In the new criteria set, classification as "definite RA" is based on the confirmed presence of synovitis in at least 1 joint, absence of an alternative diagnosis that better explains the synovitis, and achievement of a total score of 6 or greater (of a possible 10) from the individual scores in 4 domains: number and site of involved joints (score range 0–5), serologic abnormality (score range 0–3), elevated acute-phase response (score range 0–1), and symptom duration (2 levels; range 0–1).

Conclusion.
This new classification system redefines the current paradigm of RA by focusing on features at earlier stages of disease that are associated with persistent and/or erosive disease, rather than defining the disease by its late-stage features. This will refocus attention on the important need for earlier diagnosis and institution of effective disease-suppressing therapy to prevent or minimize the occurrence of the undesirable sequelae that currently comprise the paradigm underlying the disease construct "rheumatoid arthritis."

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Target population

Who should be tested ? :
Patients who

1. have at least 1 joint with definite clinical synovitis (swelling)*
2. with the synovitis not better explained by another disease†

Classification criteria for RA (score-based algorithm: add score of categories.....A–D ; a score of **≥6/10** is needed for classification of a patient as having definite RA)‡	
A. Joint involvement §	
1 large joint¶	**0**
2-10 large joints	**1**
1-3 small joints (with or without involvement of large joints)#	**2**
4-10 small joints (with or without involvement of large joints)	**3**
>10 joints (at least 1 small joint)**	**5**
B. Serology (at least 1 test result is needed for classification)††	
Negative RF *and* negative ACPA	**0**
Low-positive RF *or* low-positive ACPA	**2**
High-positive RF *or* high-positive ACPA	**3**
C. Acute-phase reactants (at least 1 test result is needed for classification)‡‡	
Normal CRP *and* normal ESR	**0**
Abnormal CRP *or* abnormal ESR	**1**
D. Duration of symptoms§§	
<6 weeks	**0**
≥6 weeks	**1**

The criteria are aimed at classification of newly presenting patients.

- In addition, patients with erosive disease typical of rheumatoid arthritis (RA) with a history compatible with prior fulfillment of the 2010 criteria should be classified as having RA.

- Patients with longstanding disease, including those whose disease is inactive (with or without treatment) who, based on retrospectively available data, have previously fulfilled the 2010 criteria should be classified as having RA.

Differential diagnoses vary among patients with different presentations, but may include conditions such as systemic lupus erythematosus, psoriatic arthritis, and gout. If it is unclear about the relevant differential diagnoses to consider, an expert rheumatologist should be consulted.

Although patients with a score of <6/10 are not classifiable as having RA, their status can be reassessed and the criteria might be fulfilled cumulatively over time.

Synovitis :

- Joint involvement refers to any *swollen* or *tender* joint on examination, which may be confirmed by imaging evidence of synovitis.

- Distal interphalangeal joints, first carpometacarpal joints, and first metatarsophalangeal joints are *excluded from assessment*.

Categories of joint distribution are classified according to the location and number of involved joints, with placement into the highest category possible based on the pattern of joint involvement.

- "Large joints" refers to shoulders, elbows, hips, knees, and ankles.

- "Small joints" refers to the metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists.

In this category,

- at least 1 of the involved joints must be a small joint; the other joints can include any combination of large and additional small joints,
- as well as other joints not specifically listed elsewhere (e.g., temporomandibular, acromioclavicular, sternoclavicular, etc.).

Negative , low positive & high positive for Rheumatoid factors

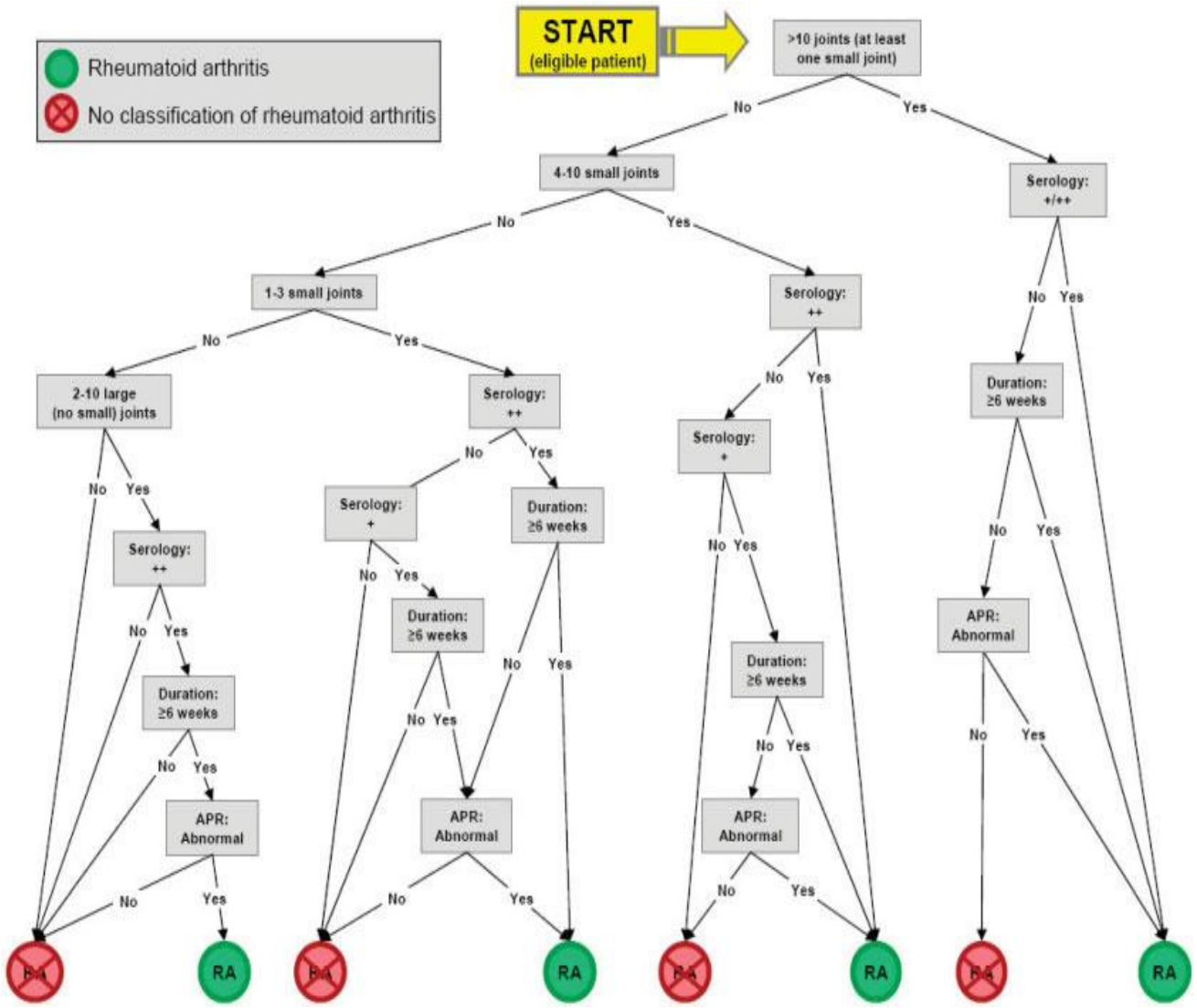
- Negative refers to IU values that are less than or equal to the upper limit of normal (ULN) for the laboratory and assay;
- low-positive refers to IU values that are higher than the ULN but ≤3 times the ULN for the laboratory and assay;
- high-positive refers to IU values that are >3 times the ULN for the laboratory and assay.
- Where rheumatoid factor (RF) information is only available as positive or negative, a positive result should be scored as low-positive for RF. ACPA = anti-citrullinated protein antibody.

Normal / abnormal for CRP & ESR

- It is determined by local laboratory standards. CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.

Duration of symptoms

- refers to patient self-report of the duration of signs or symptoms of synovitis (e.g., pain, swelling, tenderness) of joints that are clinically involved at the time of assessment, regardless of treatment status.



Tree algorithm for classifying definite rheumatoid arthritis (RA) (green circles) or for excluding its current presence (red circles) among those who are eligible to be assessed by the new criteria. APR _ acute-phase response. Serology: _ _ low-positive for rheumatoid factor (RF) or anti–citrullinated protein antibody (ACPA); serology: __ _ high-positive for RF or ACPA; serology: _/__ _ serology either _ or __. See footnotes to previous Table for further explanation of categories.

Criteria for diagnosis of Adult Still's Disease

Major Criteria

- Temperature of 39 degree of centigrade for > 1 week
- Leukocytosis > 10.000 / mm3 with > 80% PMNs
- Typical rash
- Arthralgias > 2 weeks

Minor Criteria

- Sore throat
- Lymph node enlargement
- Splenomegaly
- Liver dysfunction (high AST / ALT)
- Negative ANA , RF

- The diagnosis of adult-onset Still,s disease still remains one of exclusion , despite the unusually elevated ferritin levels in serum

- In numerous series , the previous criteria have more than 90% sensitivity

- After excluding other diseases , adult Still,s should be considered if five criteria (more than two being major ones) are met

It is not known yet whether adding hyperfirritinemia would increase the specificity of diagnosis

Sjogren,s Syndrome (SS)

European-American Consensus Group Modification of the European Community Criteria for Sjogren,s Syndrome (SS)

1-Symptoms of Dry Eye

- Patients must have a positive response to at least one of the following :
- Have you had daily ,persistent troublesome dry eyes for more than 3 months?
- Do you have a recurrent sensation of sand or gravel in the eyes ?
- Do you use tear substances more than 3 times a day ?

2-Oral Symptoms :

- Patients must have a positive response to at least one of the following :
- Have you had a daily feeling of dry mouth for more than 3 months ?
- Have you had recurrently or persistently swollen salivary glands as an adult ?
- Do you frequently drink liquids to aid in swallowing dry food ?

3-Ocular signs

- Patient must have objective evidence of ocular involvement , defined as positive result from at least one of the following two tests :
- 1-Schirmer,s test performed without anaesthesia (5 mm in 5 min)
- 2-Rose Bengal Score or other ocular dye score (4 according to van Bijsterveld,s scoring system)

4-Histopathology

- This criterion is met if in patient,s minor salivary glands (obtained through normal-appearing mucosa) focal lymphocytic sialadinitis is evaluated by an expert histopathologist withb a focus score of 1 .
- This score is defined as the number of lymphocytic foci adjacent to normal-appearing mucous acini & containing more than 50 lymphocytes / 4 mm2 of glandular tissue

5-Salivary gland involvement

- Patient must have objective evidence of salivary gland involvement defined by a positive result for at lest one of the following diagnostic tests :
- 1-Unstimulated whole salivary flow (1.5 ml in 15min.)
- 2-parotid sialography showing the presence of diffuse sialectasis , punctuate , cavitary or destructive pattern) without evidence of obstruction in the major ducts
- 3-Salivary scintigraphy showing delayed uptake , reduced concentration , delayed excretion of tracer or some combination of these

6-Autoantibodies

- Patient must have presence in the serum of the following autoantibodies :
- 1-Antibodies to Ro (SS-A) or La (SS-B)

Definite SS requires the presence of four criteria , one of them must be either positive biopsy or autoantibodies

Exclusions :

- Prior head & neck radiation ,
- Hepatitis C infection
- HIV or AIDS
- Pre-existing lymphoma
- Sarcoidosis
- Graft – versus – host disease
- Use of anti-cholinergic drugs

ANA in Sjogren,s Syndrome

Antibody specificity	**Prevalence (%)**
Ro/SS-A	40-95
La/SS-B	87
Fodrin	64-100
Proteasome	39
MA-1	8
pp75 (Ro-associated protein)	6
Kinetochore	4
p80-collin	4

EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs

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Treatment of rheumatoid arthritis (RA) may differ among rheumatologists and currently, clear and consensual international recommendations on RA treatment are not available. In this paper recommendations for the treatment of RA with synthetic and biological disease-modifying antirheumatic drugs (DMARDs) and glucocorticoids (GCs) that also account for strategic algorithms and deal with economic aspects, are described. The recommendations are based on evidence from five systematic literature reviews (SLRs) performed for synthetic DMARDs, biological DMARDs, GCs, treatment strategies and economic issues. The SLR-derived evidence was discussed and summarised as an expert opinion in the course of a Delphi-like process. Levels of evidence, strength of recommendations and levels of agreement were derived. Fifteen recommendations were developed covering an area from general aspects such as remission/low disease activity as treatment aim via the preference for methotrexate monotherapy with or without GCs vis-à-vis combination of synthetic DMARDs to the use of biological agents mainly in patients for whom synthetic DMARDs and *tumour necrosis factor* inhibitors had failed. Cost effectiveness of the treatments was additionally examined. These recommendations are intended to inform rheumatologists, patients and other stakeholders about a European consensus on the management of RA with DMARDs and GCs as well as strategies to reach optimal outcomes of RA, based on evidence and expert opinion.

Recommendations for the management of rheumatoid arthritis with non-biological and biological disease-modifying antirheumatic drugs.

Overarching principles

A Rheumatologists are the specialists who should primarily care for patients with RA

B Treatment of patients with RA should aim at the best care and must be based on a shared decision between the patient and the rheumatologist

C RA is expensive in regards to medical costs and productivity costs, both of which should be considered by the treating rheumatologist.

Final set of 15 recommendations for the management of RA

1 Treatment with synthetic DMARDs should be started as soon as the diagnosis of RA is made

2 Treatment should be aimed at reaching a target of remission or low disease activity as soon as possible in every patient; as long as the target has not been reached, treatment should be adjusted by frequent (every 1–3 months) and strict monitoring

3 MTX should be part of the first treatment strategy in patients with active RA

4 When MTX contraindications (or intolerance) are present, the following DMARDs should be considered as part of the (first) treatment strategy: leflunomide, SSZ or injectable gold

5 In DMARD naïve patients, irrespective of the addition of GCs, synthetic DMARD monotherapy rather than combination therapy of synthetic DMARDs may be applied

6 GCs added at low to moderately high doses to synthetic DMARD monotherapy (or combinations of synthetic DMARDs) provide benefit as initial short-term treatment, but should be tapered as rapidly as clinically feasible

7 If the treatment target is not achieved with the first DMARD strategy, addition of a biological DMARD should be considered when poor prognostic factors are present; in the absence of poor prognostic factors, switching to another synthetic DMARD strategy should be considered

8 In patients responding insufficiently to MTX and/or other synthetic DMARDs with or without GCs, biological DMARDs should be started*; current practice would be to start a TNF inhibitor (adalimumab, certolizumab, etanercept, golimumab, infliximab)† which should be combined with MTX*

9 Patients with RA for whom a first TNF inhibitor has failed, should receive another TNF inhibitor, abatacept, rituximab or tocilizumab

10 In cases of refractory severe RA or contraindications to biological agents or the previously mentioned synthetic DMARDs, the following synthetic DMARDs might be also considered, as monotherapy or in combination with some of the above: azathioprine, ciclosporin A (or exceptionally, cyclophosphamide)

11 Intensive medication strategies should be considered in every patient, although patients with poor prognostic factors have more to gain

12 If a patient is in persistent remission, after having tapered GCs, one can consider tapering biological DMARDs‡, especially if this treatment is combined with a synthetic DMARD

13 In cases of sustained long-term remission, cautious titration of synthetic DMARD dose could be considered, as a shared decision between patient and doctor

14 DMARD naïve patients with poor prognostic markers might be considered for combination therapy of MTX plus a biological agent

15 When adjusting treatment, factors apart from disease activity, such as progression of structural damage, comorbidities and safety concerns should be taken into account

Guidelines for the management of Rheumatoid arthritis 2002 update

American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines Arthritis & Rheumatism Vol 46. 2. February 2002 . pp 128 -346

The following guidelines for the management of RA assume that a correct diagnosis has been made & this may be difficult in the early stages of the disease

The complexity of the process needed to establish the diagnosis of RA is beyond the scope of these guidelines

These revised guidelines are evidence-based . However because significant gaps in our knowledge still exist , some recommendations are based on best practices & consensus of the committee.

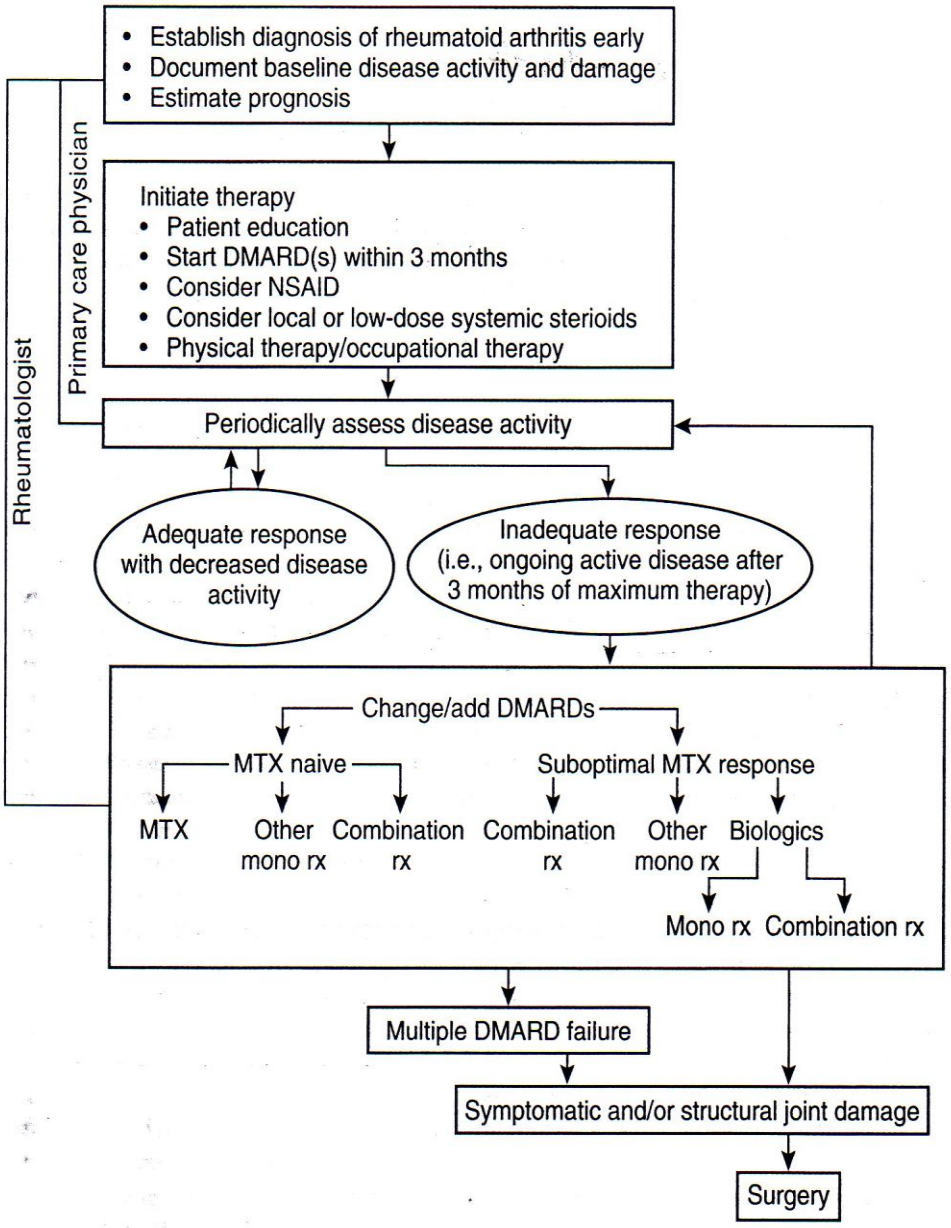
Goals of RA management

The ultimate goals in managing RA are to

- Prevent or control joint damage
- Prevent loss of function &
- Decrease pain

The following Figure summarizes the approach to the management of RA

ACR TREATMENT ALGORITHM



The initial steps in the management of RA are
(first box in the figure)

1- To establish the diagnosis ,
2- Perform baseline evaluation &
3- Estimate the prognosis

1- To establish the diagnosis

1988 Revised American Rheumatism Association Criteria for Classification of Rheumatoid arthritis

2- To perform a baseline evaluation

Baseline evaluation of disease activity & damage in patients with RA :

Subjective

- Degree of joint pain
- Duration of morning stiffness
- Duration of fatigue
- Limitation of function

Physical examination

- Actively inflamed joint (tender & swollen joint counts)
- Mechanical joint problems : loss of motion , crepitus , instability , malalignment &/or deformity
- Extra-articular manifestations

Laboratory

- ESR / CR protein level
- Rheumatoid factor
- Complete Blood Cell Count
- Electrolyte levels
- Creatinine level
- Hepatic enzyme level (SGOT , SGPT , AP) & Albumin
- Urinalysis
- Synovial fluid analysis
- Stool

Other

- Functional status or quality of life assessments using standardized questionnaire
- Physician,s global assessment of disease activity
- Patient,s global assessment of disease activity

Radiography

- Radiographs of selected involved joints

3- Estimate the prognosis

Selection of the treatment regimen requires an assessment of prognosis

Poor prognosis is suggested by

- Earlier age at disease onset
- High titer of Rheumatoid factor
- Elevated ESR &
- Selling of > 20% joints

Worse prognosis may be indicated by extra-articular manifestations such as :

- Rheumatoid nodules
- Sjogren,s syndrome
- Episcleritis & scleritis
- Interstitial lung disease
- Pericardial involvement
- Systemic vasculitis &
- Felty,s syndrome

Studies have shown that patients with

- Active ,
- Polyarticular
- RF positive

Have a > 70% probability of developing joint damage or erosion within 2 years of the onset of the disease

Since studies have demonstrated that treatment with DMARDs may alter the disease course in patients with recent onset RA , particularly those with unfavorable prognostic factors , aggressive treatment should be initiated as soon as the diagnosis has been established

The Figure : as mentioned in first box : before initiating therapy , we have to establish diagnosis , document baseline disease activity & damage and estimate prognosis

In the second box : initiate treatment with

1- Patient education
2- Start DMARDs within (3) months
3- Consider NSAIDs
4- Consider local or low dose systemic steroids
5- Physical therapy / occupational therapy

1- Patient Education

Optimal management of RA involves more than pharmacologic therapy

Early in the course of the disease , the patients needs to learn to accept that he or she will be living with RA & will need to become involved in the process of making decisions about treatment

If treatment does not fully control the disease , the patient may struggle emotionally as well as physically in adjusting to this chronic disease , its flare & the concomitant loss of function

Instruction in joint protection , conservation of energy & a home program of joint range of motion & strengthening exercises are important in achieving the treatment goal of maintaining joint function

2- Start DMARDs within 3 months

All patients with RA are candidates for DMARDs therapy

- The initiation of DMARD therapy should not be delayed beyond 3 months for any patient with an established diagnosis who despite adequate treatment with NSAIDs , has ongoing joint pain , significant morning stiffness or fatigue , active synovitis , persistent elevation of ESR or CRP level or radiographic joint damage
- For any untreated patient with persistent synovitis & joint damage , DMARD treatment should be started promptly to prevent or slow further damage

The DMARDs commonly used in RA , summarized in the following table :

Drug	Approximate time to benefit	Usual maintenance dose
Hydroxychloroquine	2-6 months	200mg twive a day
Sulfasalazine	1 – 3 months	1,000 mg 2-3 times a day
Methotrexate	1 – 2 months	Oral 7.5-25mg/week Injectable 7.5-20mg/week
Leflunomide	4 – 12 weeks	20mg/day in a single dose , if tolerated otherwise 10mg/day
Etanercept	A few days to 12 weeks	25mg subcutaneously twice a week
Infliximab plus oral & subcutaneous methotrexate	A few days to 4 months	3-10 mg IV every 8 weeks or 3-5 mg IV every 4 weeks
Azathiprine	2 – 3 months	50 -150mg /day
D-penicillamine	3 – 6 months	250 – 750 mg / day
Gold – oral	4 – 6 months	3mg twice a day
Gold – IM	3 – 6 months	25-50 mg IM every 2-4 weeks
Minocycline	1 – 3 months	100 mg twice a day
Cyclosporine	2 – 4 months	2.5-4mg / kg / day
Staphylococcal protein A immunoadsorption	3 months	Weekly for 12 weeks

Many factors influence the choice of DMARD for the individual patient

Patients & their physicians must select the initial DMARD(s) based on :

- its relative efficacy ,
- convenience of administration ,
- requirements of the monitoring program ,
- costs of the medication & monitoring (including physician visits & laboratory costs)
- time until expected benefit &
- the frequency & potential seriousness of adverse reactions

The physician should also assess patient factors , such as likelihood of compliance , comorbid disease , severity & prognosis of the patient,s disease & the physician,s own confidence in administering & monitoring the drug

For women of childbearing age , effective contraception is required when most DMARDs are prescribed
The drug regimen will need to be modified if pregnancy or breastfeeding is contemplated

Bases on considerations of safety , convenience , & cost , many rheumatologists select HCQ or SAZ first , but for the patient with very active disease or with indicators of poorer prognosis , MTX or combination therapy would be preferred

MTX as monotherapy or as a component of combination therapy should be instituted in patients whose treatment has not yet included MTX .

For patients in whom MTX is contraindicatd or as failed to achieve satisfactory disease control either because of the lack of efficacy (in doses up to 25mg/week) or intolerance , treatment with biologic agents or with other DMARDs , either alone or in combination , is indicated

Htdroxychloroquine (HCQ)

- Although HCQ alone does not slow radiologic damage , early treatment with HCQ has a significant impact on long-term patient outcome
- HCQ is generally well tolerated & requires no routine laboratory monitoring , although patient need periodic ophthalmologic examination for early detection of reversible retinal toxicity
- The risk of retinal toxicity is increased when the dose exceeds 6mg/kg
- The length of time to benefit may vary from 1 month to as long as 6 months

Salazopyrine or sulfasalazine (SAZ)

- It may act more quickly than HCQ , with benefit sometimes as early as 1 month after beginning therapy

- It retard radiographic progression of RA
- It is usually well tolerated , with most side effects , which include nausea & abdominal discomfort , occurring in the first few months of therapy
- The incidence of these side effects is lessened by starting at a low dosage & then gradually increasing the dosage
- Leukopenia is an occasional , more serious side effect that occur at any time & periodic laboratory monitoring is therefore necessary
- Clinical response should be apparent within 4 months , the need for a change in therapy may be determined at that time

Methotreate (MTX)

- Many rheumatologists select MTX as the initial DMARD , especially for patients whose RA is more active

- Because of its favorable efficacy & toxicity profile , low cost & established track record in the treatment of RA … MTX has become the standard by which new DMARDs are evaluated

- It retard the progression of radiographic erosions
- More than 50% of patients who take MTX continue the drug beyond 3 years , which is longer than any other DMARD

- RA patients taking MTX are more likely to discontinue treatment because of adverse reactions than because of lack of efficacy

- Relative contraindications for MTX therapy are preexisting liver disease , renal impairment , significant lung disease or alcohol abuse
- Since the most frequent adverse reaction to MTX is elevation of liver enzyme levels , liver function must be monitored , but the risk of liver toxicity is low

- Rare , but potentially serious & even life-threatening pulmonary toxicity may occur at any time with any dosage of MTX

- Lymphoproliferative disorders may rarely occur in patients taking MTX

- Since MTX is potentially teratogenic appropriate contraceptive measures during MTX treatment are recommended

Leflunomide

- It is an alternative to MTX as monotherapy , especially for patients who cannot tolerate MTX o inadequate response

- It is also beneficial as combination therapy with MTX , in the absence of a complete clinical response with full doses of MTX

- It elevate liver enzymes
- It is potent teratogen

- It is contraindicated in : obstructive biliary disease , liver disease , viral hepatitis , severe immunodeficiency , inadequate birth control & rifampin therapy (which rises its serum levels)

Anti-TNF alpha

TNF antagonists

- Two anti-TNF alpha agents are available in Egypt now : Etanercept & Infliximab

- Both have been shown to be beneficial when used in combination with MTX in patients with ongoing active RA despite adequate doses of MTX alone

- Infliximab is currently recommended for use only with concomitant MTX therapy
- For both agents , many patients improved rapidly , even during the first 2 weeks of treatment

- Patients treated with Etanercept alone or with Infliximab plus MTX have less radiographic progression after 1 year than patients treated with MTX alone

- They should be used with caution in patients with any susceptibility to infection or a history of TB , should be avoided in patients with significant chronic infections , & should be discontinued temporarily in all patients with active infection

- In addition to the absence of long-term safety data , the disadvantages of TNF antagonists are the need for parenteral administration & the high cost of these medications

- Not all patients with RA respond to these agents & disease flares occur after therapy is discontinued

Older DMARD

Azathioprine (AZA)

- It has demonstrated benefits in controlling RA , but it is rarely used

D-penecillamine

- It is , but its use is limited , in part by an inconvenient dosing & serious side effects

Intramuscular Gold

- it is effective
- But injections are required every week for 22 weeks before less-frequent maintenance dosing is initiated
- Although oral gold is more convenient than injectable gold , there is a long delay (up to 6 months) before benefits are evident & it is less efficient

Tetracyclines

- Recently , it is demonstrated that Minocycline is efficient in improving the clinical parameters of RA

Cyclosporine

- It is beneficial as monotherapy
- It has short-term efficacy
- Its use is limited because of toxicity , especially hypertension & dose related loss of renal function

Staphylococcal protein A immunoadsorption

- It is efficient in a portion of patients with refractory RA
- It is difficult in administration (up to 12 weeks) , high cost , limited duration of response , high frequency of side effects
- Therefore it should be considered only in refractory RA in whom treatment with several DMARDs has failed

Combination DMARD therapy

- Monotherapy often fails to control RA , therefore prescribing combination therapy is increasing

Two strategies for combination therapy

1- **Step-up strategy** : we start with monotherapy … if no enough response (single therapy had failed) (persistently active disease) … then add another DMARD (combination)

2- **Step-down strategy** : start with combination therapy … then apply step-down approach once adequate disease control is attained

- In either case rheumatology referral is strongly recommended for patients being considered for initiation of combination therapy

- The triple – DMARD combination of MTX , HCQ & SAZ has substantially increased efficacy compared with MTX alone & with the combination of HCQ plus SAZ without increased toxicity

- Recently : the triple – DMARD combination of MTX , SAZ & HCQ has been shown to be superior to the double – DMARD combinations of MTX plus SAZ or MTX plus HCQ in both early & more advanced RA

- Over the last several years , combination DMARD therapy has played a significant role in improving our ability to control RA .The role of combination DMARD therapy continues to evolve

3- Consider NSAIDs

- These agents have analgesic & anti-inflammatory properties but do not alter the course of the disease or prevent joint destruction
- Thus they should not be used as the sole treatment for RA
- Patients with RA are nearly twice as likely as patients with OA to have a serious complications from NAID treatment

Risk factors for the development of NSAID-associated gastrointestinal (GI) ulcers include :

- Advanced age (> 75 years)
- History of ulcer
- Concomitant use of corticosteroids or anticoagulants
- Higher dosage of NSAIDs
- Use of multiple NSAIDs or
- A serious underlying disease

The following approaches may be considered for patients with RA who would benefit from an NSAID but who are at increased risk of serious adverse GI effects

- Use of low-dose prednisone instead of an NSAID
- Use of a nonacetylated salicylate
- Use of a highly selective COX-2 inhibitor
- Use of a combination of an NSAID & A gastroprotective agent (high-dose H2 blockers , proton-pump inhibitors & oral prostaglandin analogs

While symptoms of dyspepsia are often improved by treatment with H2 blockers , one study showed that asymptomatic patients with RA who were receiving both NSAID & low-dose H2 blockers were at higher risl of GI complications than those receiving NSAIDs alone
Therefore routine use of H2 blockers to prevent dyspepsia or to protect against NSAID-induced gastropathy is not recommended

Use of NSAIDs & selective COX-2 inhibitors , should be avoided in conditions associated with diminished intravascular volume or edema , such as congestive heart failure , nephrotic syndrome , or cirrhosis & in patients with serum creatinine levels > 2.5mg/dl

4- Consider Glucocorticoids (GCs)

- Low-dose oral GCs (10 mg of prednisone daily or the equivalent) & local injections of GCs are highly effective for relieving symptoms in patients with active RA
- Frequently , disabling synovitis recurs when GCs are discontinued , even in patients who are receiving combination therapy with one or more DMARDs … therefore , many patients with RA are functionally dependent on GCs & continue them long-term

- Recent evidence suggests that low-dose GCs slow the rate of joint damage & therefore appear to have disease – modifying potential … joint damage may increase on discontinuation of GCs
- The beneficial of low-dose systemic GCs , however , should always be weighted against their adverse effects
- For long-term disease control , the GC dosage should be kept to a minimum … For the majority of patients with RA , this means < 10 mg of prednisone per day

- RA is associated with an increased risk of osteoporosis independently of GC therapy
- Patients taking GCs at dosage as low as 5mg/day have an increased risk of osteoporosis , densitometry to assess bone loss should be performed at regular intervals for the duration of GC treatment
- GC-treated patients should receive 1500 mg of elemental Calcium per day (including diet & supplement) & 400-800 IU of vitamin D per day

- GC injection of joints & periarticular structures is safe & effective when administered by an experienced physician
- Injecting one or a few of the most involved joints early in the course of the RA may provide local & even systemic benefit
- The effects are sometimes dramatic , but temporary
- A patient who has disease flare in only one or a few joints can be treated successfully by injecting the particular joint(s) , without requiring a major change in the prescribed treatment regimen

Not all joint flares in RA patients are caused by the disease

- Joint infection or microcrystalline arthritis must be considered & ruled out before local GC injections are given

- In general , the same joint should not be injected more than one within 3months
- The need for repeated injections in the same joint or for injections for multiple joints indicates the need for reassess the adequacy of the overall treatment program

6- Physical therapy / Occupational therapy

They may help the patient who is compromised in activities of daily living
Regular participation in dynamic & even aerobic conditioning exercise programs improves joint mobility , muscle strength , aerobic fitness & function & psychological well being without increasing fatigue or joint symptoms

Monitoring of toxicities of drugs used to treat Rheumatoid arthritis

Drug category	Toxicities requiring monitoring	Baseline evaluation	Systems review	Laboratory
Salicylates : NSAIDs	GI ulceration & bleeding	CBC , creatinine , LFTs	Dark/black stool , ,dyspepsia , nausea , vomiting , abdominal pan , edema , shortness of breath	CBC yearly , LFTs
Hydroxychloroquine	Macular damage	None unless patient is over age 40 or has previous eye disease	Vision changes , funduscopic & visual fields every 12 months	None
Sulfasalazine	Myelosuppression	CBC & LFTs in patients at risk. G6PDH	Myelosuppression & photosensitivity , rash	CBC every 2-4 weeks for first 3 months then every 3 months thereafter
Methotrexate	Myelosuppression , hepatic fibrosis,	CBC , creatinine	Myeosuppression & shortness of	CBC , creatinine ,

	cirrhosis , pulmonary infiltrates or fibrosis	LFTs , Chest X-ray , within previous year. Hepatitis B & C serology in high risk patients	breath. Nausea / vomiting . lymph node swelling . Potentially teratogenic	LFTs monthly for the first 6 months ; every 2 months thereafter , For minor elevation in AST or ALT (< 2fold ULN) repeat testing in 2-4 weeks , For moderate elevation s in AST or ALT (> 2 fold ULN) discontinue MTX & perform liver biopsy as necessary
Leflunomide	Diarrhea , alopecia rash , headache , theoretical risk of immunosuppression infection	Hepatitis B & C serology in high risk patients CBC , creatinine , LFTs	Diarrhea , alopecia , intercurrent liver. Gallbladder , renal disease , pregnancy or delayed menses , Known teratogen	CBC , creatinine , LFTs monthly for the first 6 months : every 1-2 months thereafter , For minor elevations in AST or ALT (< 2 folf ULN) repeat testing in 2-4 weeks . For moderate elevations in AST or ALT (> 2 fold ULN < 3 fold ULN) closely monitor with LFTs every 2-4 weeks & dosage reduction . For persistent elevations of AST or ALT (>

				2 or 3 fold) discontinue Leflonamide & eliminate with Cholestyramine therapy : performs liver biopsy as necessary . Patients also taking MTX should have LFTs at least monthly
Etanercept	None recognized	Assess for infection or risk factors for infections	Acute or chronic infections	Monitor for infection site reactions
Infliximab plus MTX	None recognized	Assess for infections or risk factors for infections	Acute or chronic infections	Monitor for infusion reactions & see MTX above
Azathioprine	Myelosuppression , hepatotoxicity , lymphoproliferative disorders	CBC , creatinine , LFTs	Myelopsuppression	CBC every 1-2 weeks with changes in dosages & in every 1-3 months thereafter
D-pnicillamine	Myelosuppression , proteinuria	CBC m creatinine , urinary protein (dipstick)	Myelosuppression , edema , rash	CBC , urinary protein (dipstick) every 2 weeks until dosage stable , then every 1-3 months
Gold (IM)	Myelosuppression , proteinuria	CBC , creatinine , urinary	Myelosuppression , edema , rash , oral ulcers , diarrhea	CBC , urinary protein (

		protein		dipstick) every 1-2 weeks for first 20 weeks , then at time of each (or for every other) injection
Gold (oral)	Myelosuppression , proteinuria	CBC , urinary protein (dipstick)	Myelosuppression , edema , rash , diarrhea	CBC , urinary protein (dipstick) every 4 -12 weeks
Minocycline	Hyperpigmentation , dizziness , vaginal yeast infections	None	Hyperpigmentation , dizziness , vaginal yeast infections	None
Cyclosporine	Renal insufficiency , anemia , hypertension	CBC , creatinine , LFTs , uric acid m BP	Hypertichosis , paresthesia , nausea , gingival hyperplasia , edema , BP every 2 weeks until dosage stable , then monthly thereafter	Creatinine every 2 weeks until dosage is stable , then monthly : periodic CBC , LFTs & potassium
Glucocorticoids (oral < 10mg/day of prednisone)	Hypertension , hyperglycemia , osteoporosis	BP , blood chemistries panel , bone densitometry in high risk patients	Polyuria , polydipsia , edema , shortness of breath , vision changes , weight gain , fracture , BP at each visit	Urinalysis for glucose yearly

LFTs = Liver function tests

Now , you diagnose your patients (first box of the figure) , & you initiate the optimum therapy (box two in the figure) ,& we have to follow up our patients (proceed to the third box)

At each follow up visit , the physician must assess whether the disease is active or inactive

Assessment of disease activity in RA

At each visit , evaluate for subjective & objective evidence of active disease

- Degree of joint pain (visual analogue scale)
- Duration of morning stiffness
- Duration of fatigue
- Presence of actively inflamed joints on examination (tender & swollen joint counts)
- Limitation of function

Periodically evaluate for disease activity or disease progression

- Evidence of disease progression on physical examination (loss of motion , instability , malalignment &/or deformity)
- ESR or CRP elevation
- Progression of radiographic damage of involved joints

Other parameters for assessing response to treatment (outcomes)

- Physician,s global assessment of disease activity
- Patient,s global assessment of disease activity
- Functional status or quality of life assessment using standardized questionnaires

The american College of Rheumatology (ACR) has developed criteria for defining improvement & clinical remission in RA

These criteria have become accepted for outcome assessment in clinical trials , but have not been widely adopted for clinical practice

The ACR criteria for 20% clinical improvement (The ACR 20) require a (20%) improvement in the tender & swollen joint count , as well as a (20%) improvement in 3 of the following 5 parameters

- Patient,s global assessment
- Physician,s global assessment
- Patient,s assessment of pain
- Degree of disability &
- Level of acute phase reactant

These criteria have been expanded to include criteria for 50% & 70% improvement measures (i.e. ACR 50 , ACR 70)

Some patients have resistant disease & experience a progressive course despite exhaustive trials of DMARDs , whether used alone or in combinations

While the ultimate goal of treating RA is to induce a complete remission , this occurs infrequently

Complete remission is defined as the absence of the following :

1- Symptoms of active inflammatory joint pain (in contrast to mechanical joint pain)
2- Morning stiffness
3- Fatigue
4- Synovitis on joint examination
5- Progression of radiographic damage on sequential radiographs
6- Elevation of the ESR or CRP levels

- If complete remission is not achieved , the management goals are to control disease activity , alleviate pain , maintain function for activities of daily living & work , maximize quality of life

- Achieving these goals challenges the management skills of the rheumatologists to determine the most efficacious combination of pharmacologic therapy , which may include NSAID , DMARD(s) , low-dose steroids , local injection o GC , rehabilitation support & analgesics

Although adequate pain relief is an important goal with a chronic disease such as RA , every effort should be made to avoid narcotic analgesic dependency

Surgical treatment of RA

- In patients who have unacceptable levels of pain , loss of motion , or limitation of function because of structural joint damage , surgical procedures should be considered

In early 2005 ,

- The ACR determined that it was necessary to add the following information to these treatment guidelines

- Some recent placebo controlled trials show an increased risk of thrombotic cardiovascular events , including non-fatal myocardial infarction & non-fatal strokes , with COX-2 selective NSAIDs , particularly when used at higher doses

Physicians & patients should weight the potential risks & benefits of treatment with these modalities , as with all drugs

Juvenile Rheumatoid Arthritis

Hypothetical Sequence of Medical Therapy in Children with JRA

James T. Cassidy ; Rheumatic diseases of childhood , section XV , Juvenile Rheumatoid arthritis , chapter 96 , P:1579-1596 , Kelleys textbook of Reumatology ,seventh edition ; 2005

Guidelines for management of JRA

- It is virtually important that the parent & the child , if cognitively possible , understand the disease & share in its management .
- A considerable amount of time & effort must be expanded in explaining the nature of JRA , reasonable expectations during initial therapy , & the course of the disease
- These educational efforts must be ongoing process
- Attendance at school is strongly encouraged ; only rarely is home instruction indicated

The philosophy of management is :

- To begin with the simplest , safest & most conservative measures
- If this approach proves inadequate , the physician should choose other therapeutic modalities in an orderly fashion
- Therapy is generally continued for 1 to 2 years after all manifestations of the disease activity have been suppressed to avoid the error of stopping anti-inflammtory therapy during short , self-limiting remissions

- In children : potentially toxic regimens such as prolonged steroid use & immunosuppressive drugs should be employed only for Life-threatening disease
- Nutrition is an important aspect of long-term management … dietary supplementation is often wise , especially with vitamin D & calcium

Addition of medications & alteration of the therapeutic plan are based on the type of onset & course of the disease , its activity & severity , & the clinical response to each sequential therapeutic maneuver

The following Algorithm to demonstrate the sequence of events & the suggested measure for type of JRA , first oligarticular type , then polyarticular & lastly systemic onset tyope of JRA

Oligoarthritis

NSIADs

Hydroxychloroquine

IA steroid

Methotrexate

Sulfasalazine
IM gold

Polyarthritis

NSAIDs

Methotrexate
TNFR:FC
Prednisone

Hydroxychloroquine

IA steroids

IVIG
IM gold
Sulfasalazine
Cyclopsporine

Azathioprine
Cycphosphamide

Experimental therapy

Autologous stem cell transplantation

Systemic disease

NSAIDs
Prednisone

IV steroid pulse

Methotrexate

IA steroid

Cycosporine
IVIG

AZAthioprine
Cycophosphamide

Experimental therapy

Autologous tem cell transplantation

NSAIDs

- Aspirin : treatment started at 75 to 90 mg / kg / day (depending on the child,s age & weight) , given in divided dose four time a day with meals & at bed time with milk to minimize gastrointestinal irritation

Among NSAIDs approved for use in North America

- Naproxen : 15 to 20 mg / kg / day twice daily
- Ibuprofen : 35 mg / kg / day four times daily
- Tolmetin : 25 mg / kg / day four times daily

Methotrexate

- When children do not respond adequately to an initial trial of NSAIDs , a number of other medications should be considered as additions to the antirheumatic program
- Methotrexate (MTX) is currently the most frequently prescribed drug in children who have failed to respond to NSAIDs

- MTX should be avoided in children with risk factors such as malnutrition , viral hepatitis , diabetes mellitus , obesity , smoking , or alcohol consumption

- Folic acid is given (1 mg / day) during treatment in addition to a multivitamin

- The injectable preparation (25mg / ml) can be used orally in children to prescribe the correct amount
- The minimum starting dose is 10mg / m2 weekly (0.35 to 0.45 mg / kg / week)

- Monitoring during the course of treatment includes CBC & liver function tests every 4 to 8 weeks
- The drug should be administered subcutaneously when use in higher dosage (0.65 to 1.0 mg / kg / week) with a maximum dose of approximately 30mg / week

- MTX therapy should be continued for approximately 1 year after a sustained remission of the disease is achieved

- Tapering of the dose may include an every-two-week schedule

Glucocorticoids

- Initial control of inflammatory disease is sometimes aided by the addition of low-dose prednisone in th e morning for a short period of time (bridge therapy)

For uncontrolled systemic disease with marked disability

- Use Prednisone

- In a single morning dose of 0.1 to 1.0 mg / kg / day (less than or equal to 40 mg / total) OR in divided doses for more severe disease
- After satisfactory control is reached , the drug should be gradually decreased & eventually discontinued
- If no adequate or no response , also withdrawal should be done

- Steroid pseudorheumatism may make even slow withdrawal of the drug difficult

- Growth retardation
- It is the most significant untoward effect of steroid therapy
- A dose of 5mg/day is usually inhibitory as little as 3mg in a child weighting less than 25kg may be suppressive

To minimize the daily steroid requirement or to avoid it altogether

- IV steroid pulse therapy has been introduced for treatment of the more severe manifestations of JRA
- Methylprednisone is the drug of choice
- Dose = 10 to 30 mg / kg per pulse
- Single pulse … up to three pulses on alternate days
- Much caution … IV GCs pulse therapy can cause serious & fatal complications involving electrolyte & fluid imbalance & cardiac arrhythmia

Triamcinolone hexacetonide

- It is the long-acting intra-articular preparation preferred therapeutically for use in one or two joints that do not respond satisfactory to a conservative program or as a short term aid to physical therapy
- Dosage = 5 to 40 mg … depending on the size of the joint
- IA injections should not be given more than a limited number of times if satisfactory results are not achieved – for example , three times in a single joint during a 6-month period

Etanercept

- The controlled trial of etanercept in children with polyarticular JRA who had failed therapy with MTX indicated that 74% demonstrated improvement at 3 months on a subcutaneous dose of 0.4mg / kg twice a week
- The long term safety of TNF-alfa blockade is unknown
- It should not be used in children with recurrent or chronic infections
- Tuberculosis should always be excluded before beginning therapy

Hydroxychloroquine (HCQ)

- It is often considered a useful adjunctive therapeutic agent in the older child
- The initial dose is 5mg / kg / day (400mg total)
- An ophthalmologic examination with evaluation of color vision must be performed before institution of therapy & periodically thereafter
- The drug should be discontinued when any suspicion of retinopathy is present because its effects are cumulative

Gold compounds

- Now less frequently used since introduction of MTX
- It is given in conjunction with NSAIDs & often with HCQ
- Children with systemic –onset disease may be at greater risk for reaction from any of the medications used to treat JRA

D-penicillamine

- It is effective
- Indications for use are the same as those for gold compounds
- These two agents should not be combined therapeutically
- Maintenance dose = 10mg / kg / day … approximately 750mg/day)

Intravenous Immunoglobulin

- It has been proposed as adunjctive therapy for polyarticular & systemic-onset JRA

Sulfsalazine

- It is effective
- Relatively safe
- Response within 6 to 8 weeks
- It is contraindicated for children with hypersensitivity to sulfa , salicylate , impaired renal or hepatic function

Septic Arthritis

Guidelines for Synovial Fluid Analysis in Septic Arthritis

If you suspect a case of septic arthritis

Do diagnostic arthrocentesis
(always try to tap the joint dry)

- Note which joint
- Total volume of synovial fluid
- Gross description of fluid , bloody or non-bloody
-

If the fluid is bloody
Consider the following differential diagnosis of Hemoarthrosis

- Trauma with or without fracture
- Over anticoagulation
- Hemophilia
- Other bleeding disorders
- Pigmented villonodular synovitis or other tumors
- Traumatic tap

Then consider the WBC count
If it is > 50.000 / cmm
It is markedly inflammatory fluid :
Consider empiric antibiotic therapy pending culture results

If it is < 50.000 / cmm
It is non-inflammatory or moderately inflammatory fluid
Consider a broad differential diagnosis from OA to RA
However , septic arthritis is less likely but still possible

Ten consider crystals ?
Under polarized light microscope

If it is positive
So , it is gout or pseudogout at least
But do also gram stain & culture

If no crystals
Ask for gram stain &/or culture positive
If positive
It is septic arthritis

If it is negative
It means markedly inflammatory fluid due to crystals or infection :
Consider the other possibilities

Systemic Lupus Erythematosis

Classification of Systemic Lupus Erythematosis (SLE)

1-Malar Rash :

- Fixed erythema , flat or raised , over the malar eminences , tending to spare the nasolabial folds

2-Discoid Rash :

- Erythematous raised patches with adherent keratotic scalling & follicular plugging atrophic scarring may occur in older lesions

3-Photosensitivity :

- Skin rash as a result of unusual reaction for sunlight , by patient history or physician observation

4-Oral ulcers

- Oral or nasopharyngeal ulceration , usually painless , observed by a physician

5-Arthritis :

- Nonerosive arthritis involving two or more peripheral joints , characterized by tenderness , swelling or effusion

6-Serositis :

- A- Pleuritis : convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion
  OR
- B- Pericarditis : documented by ECS , rub or evidence of pericardial effusion

7-Renal disorder :

- A- Persistent proteinuria greater than 0.5 gram per day or greater than 3+ if quantitation not performed
  OR
- B- Cellular casts : which may be red cell , hemoglobin , granular , tubular or mixed

8-Neurologic disorder :

- A- Seizures : in absence of offending drugs or known metabolic derangements (e.g. uremia , ketoacidosis , or electrolyte imbalance)
  OR

- B- Psychosis : in the absence of offending drugs or known metabolic derangements (e.g. uremia , keratoacidosis , electrolyte imbalance)

9-Hematologic disorder :

- A- Hemolytic anemia : with reticulocytosis
- B- Leukopenia : less than 4000 / cmm total in two or more occasions
- C- Lymphopenia : less than 1500 / cmm on two or more occasions
- D- Thrombocytopenia : less than 100.000 / cmm in the absence of offending drugs

10-Immunologic disorders :

- A- Anti-DNA : antibody to native DNA in abnormal titer
  OR
- B- Anti-Sm : presence of antibody to Sm nuclear antigen
  OR
- C- Positive finding of antiphospholipid antibodies based on :
  1- an abnormal serum level of IgG or IgM anti-cardiolipin antibodies
  2- a positive test result for lupus anticoagulant using a standard method OR
  3- a false –positive serologic test for syphilis known to be positive for at least 6 months & confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody absorption test

11-Antinuclear Antibody :

- An abnormal titer of antinuclear antibody (ANA) by immunofluorescence or an equivocal assay at any point in time & in the absence of drugs known to be associated with (drug-induced Lupus) Syndrome

The fundamental rule is that a patient must have (4) or more of the (11) criteria to qualify for the classification category of SLE

Learning & remembering 11 criteria may seem a daunting task for the individual who is also learning the anatomy & physiology of all joints , muscles & tendons in the body .

Instead of considering 11 separate criteria , it may be useful to think through six logical clinical groupings :

- Joints
- Skin
- Serosal surfaces
- Kidneys
- Hematologic elements
- Neuropsychatric elements

& then finally the system that links all together : immunologic abnormalities

Granted , each of these six clinical areas has further subgroupings that need to be recalled ; however , if one pictures an (archtypical) lupus patient who has arthritis , photosensitive rash , pleurisy , proteinuria , thrombocytopenia & seizures when considering the diagnosis , the criteria will naturally follow

Antinuclear Antibodies (ANAs) in SLE

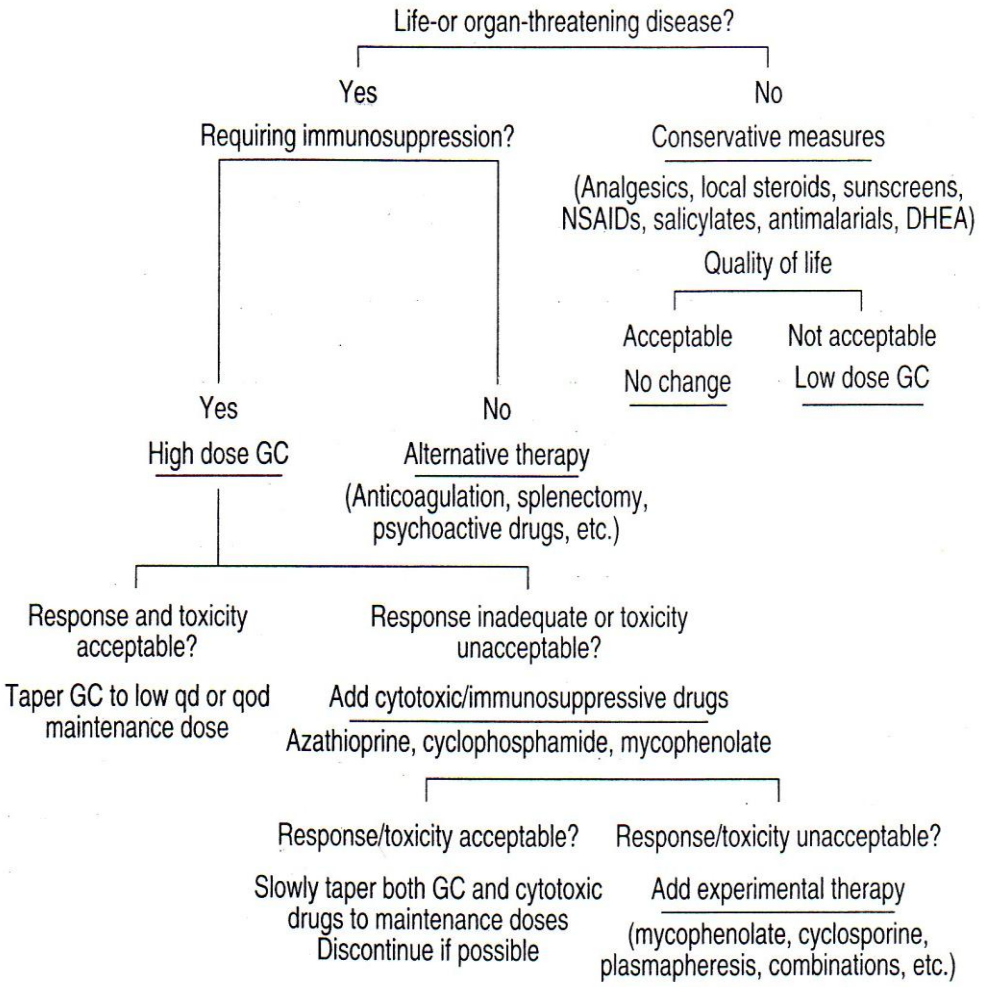
Antibody Specificity	Prevalence (%)
Chromatin-Associated antigens	
Ds-DNA	73
Histone	50-70
Chromatin	88
Ku	20-40
PCNA	3-6
RNA polymerase II	9-14
kinetochore	6
Ribonucleoproteins	
snRNPs	
Sm core	20-30
U1snRNP	30-40
U2 snRNP	15
U5 snRNP	?
U7snRNP	?
Ro/SS-A	40
La/SS-B	10-15
Ribosomes	
PO , P1 , P2 protein	10-20
28S rRNP	?
S10 protein	?
L5 protein	?
L12 protein	?
proteasome	58

Guidelines for selecting management of patients with SLE

Bevra Hannahs Hahn , management of SLE , chapter 76 , Kelley,s textbook of rheumatology ,seventh edition , 1225-1247 , 2005

Because most therapeutic interventions in patients with SLE are associated with significant undesirable side effects , the physician must first decide whether a patient needs treatment & if so , whether conservative management is sufficient or aggressive immunosuppression is necessary .

The following figure , presents an algorithm for this decision making



Let us discuss the algorithm , briefly :

If there is no life- or organ – threatening disease

Conservative measures

- Analgesics
- Local steroids
- Sunscreens
- NSAIDs
- Salicylates
- Antimalarials
- DHEA = Dihydroandrosterone , 100 : 200 mg daily

If quality of life is acceptable

- Do not change

If quality of life not acceptable

- Add low dose of GC

If there is life- or organ – threatening disease

Requiring immunosuppression
If yes
Give High dose of Glucocorticoid

If response & toxicity is acceptable

- Taper GC to low qd or qod maintenance dose

If response is inadequate or toxicity is unacceptable

- Add Cytotoxic / immunosuppressive drugs
- Azathioprine , Cyclophosphamide , Mycophenolate

If response / toxicity are acceptable

- Slowly taper both GC & cytotoxic drugs to maintenance doses
- Discontinue if possible

If response / toxicity are unacceptable

- Add experimental therapy
- Mycophenolate
- Cyclosporine
- Plasmapheresis
- Combinations …. Etc.

Serious & Life-threatening manifestations of SLE , responses to Glucocorticoids

Manifestations usually responsive to high-dose GCs

- Vasculitis
- Severe dermatitis of subacute cutaneous lupus erythematosis or SCLE
- Polyarthritis
- Polyserositis – pericarditis , pleurisy , peritonitis
- Myocarditis
- Lupus pneumonitis
- Glomerulonephritis – proliferative forms
- Hemolytic anemia
- Thrombocytopenia
- Diffuse CNS syndrome – acute confusional state , demyelinating syndromes , intractable headache
- Serious cognitive defects
- Myelopathies
- Peripheral neuropathies
- Lupus crisis – high fever & prostration

Manifestations not often responsive to GCs

- Thrombosis , includes strokes
- Glomerulonephritis – scarred end-stage renal disease , pure membranous glomerulonephritis
- Resistant thrombocytopenia or hemolytic anemia – occur in a minority of patients ; consider splenectomy , cytotoxics , danazol or cyclosporine / neural therapies
- Psychosis related to conditions other than SLE , such as GC therapy

Strategies to minimize the adverse effects of treatment with GCs or Cytotoxic drugs in patients with SLE

I : Methods of using drugs

1- Initiate use only in patients with life-threatening disease or severely impaired quality of life

2- Monitor at frequent intervals

- GCs : electrolytes , CBC count , glucose levels , evidence of infection , blood pressure , intra-ocular pressure , formation of cataracts , evidence of osteoporosis

- Cytotoxic drugs : CBC count , platelet count , liver function tests , evidence of infection , urinalysis for microscopic hematuria (with oral cyclophosphamide) , signs of malignancy

3-Reduce drug doses as frequently as possible

II : Treatment & prevention of infection

1-Be aware of the high incidence of infections , both ordinary & opportunistic , The most frequent organisms are herpes zoster , urinary tract infections with gram-negative bacteria & infection with staphylococcus , Candida (including sepsis) , Mycobacteria , Fungi & viruses such as CMV are not unusual . Monitor carefully for evidence of these

2-If infection is suspected, treat for the most likely organisms , Therapy can be discontinued or changed after culture information is available

3-Immunize to prevent infections . Annual influenza vaccination & one immunization with pneumococcal vaccine (pneumovax 23) are recommended for all patients

4-Some recurring infections can be prevented , or their frequency diminished , by use of prophylactic antibiotics

III : Correct manifestations of GC toxicity

1-Control hypertension
2-Control hypokalemia
3-Control symptomatic hyperglycemia

IV : Encourage exercises to counter the weight gain & myopathy of GC therapy

V : Minimize the osteoporosis associated with GC therapy

1- Advise adequate daily calcium intake (1000mg for premenopausal women & for men ; 1500mg for postmenopausal women)

2- If 24-hour urinary calcium excretion is less than 120mg add vitamin D , 50000 units 1-3 times weekly (or Calcitriol , 0.5 ygm) . Monitor calcium levels in serum & urine every 3-4 months if this is instituted

3- When women become menopausal , consider hormone replacement therapy if not contraindicated & LLE is stable

4- If risk for osteoporosis is high or if fractures occur , add bisphosphonates , calcitonin or teriparaide

Use of Antimalarials & Experimental Regimens to treat cutaneous Lupus :

Hydroxychloroquine (HQ)

- Initial dose = 400 to 600 mg / day
- Maintenance dose = 100-400 mg / day
- For : Dermatitis (SLE , DLE , SCLE) , Arthralgia , Arthritis , Oral ulcers , Fatigue
- Toxicities = Retinal damage , Corneal deposit , Skin pigmentation , Rashes , Alopecia , Peripherl neuropathy , Peripheral myopathy , Cardiomyopathy , nausea , anorexia , Diarrhea , Psychosis

Chloroquine :

- Initial dose = 500 mg / day for one week
- Maintenance dose = 250 mg / day OR every other day (do not exceed 4mg / kg)
- For : as for hydroxychloroquine – probably most effective for arthritis
- Toxicities : as for HQ – probably most toxic for retina

Quinacrine

- Initial dose = 100 mg / day
- Maintenance dose = 50 – 100 mg / day
- For : probably most effective for Fatigue
- Toxicities = Aplastic anemia , little or no retinal damage , yellow pigmentation of the skin

HQ OR Chloroquine + Quinacrie

- Initil dose = s indicated above
- Maintenance dose = as indicated above
- For : effects probably additive for dermatitis
- Toxicities = probably not additive

Experimental Dapsone

- Initial dose = 25 mg twice daily
- Maintenance dose = 25 mg / day
- For : Dermatitis (especially DLE & bullous LE)
- Toxicities : Methemoglobulinemia , hemolytic anemia < gastrointestinal intolerance

Etretinate

- Initial dose = 1 mg / kg / day in divided doses
- Maintenance dose = 0.25 – 0.5 mg / kg / day
- For : Dermatitis (especially DLE & SCLE)
- Toxicities : hyperlipidemia , Cheilitis , fetal abnormalities

Comments :

- For individuals with Lupus rash resistant to antimalarials & other conservative strategies , systemic therapy with tretinoids (such as isotretinoin or topical therapy with tretinoin) has been beneficial
- Patients resistant to antimalarials & retinoids may require systemic glucocorticoids , which improve Lupus skin lesions of any type
- Additional therapies which should be considered : Dapsone , Thalidomide &Tacrolimus
- Some steroid-resistant cases of Lupus dermatitis have improved when treated with Cytotoxic drugs such as Azathioprine (AZA) or MTX. MTX may be more useful

Guidelines for use of Cytotoxic Drugs in SLE in addition to Glucocorticoids (GCs)

Azathioprine (AZA)

- Initial dose = 1-3 mg / kg / day
- Maintenance dose = 1-2 mg / kg / day
- Advantage : probably reduces flares , reduces renal scaring , reduces GCs dose requirement
- Adverse side effects : bone marrow suppression , leukpenia , infection (including herpes zoster) , malignancies , infertility , early menopause , hepatic damage , nausea

Cyclophosphamide (CYC)

- Initial dose = 1-3 mg / kg / day orally or 8-20 mg / kg intravenously once a month plus mesna
- Maintenance dose = 0.5 - 2 mg / kg / day orally or 8 – 20 mg / kg intravenously every 4 – 12 weeks plus mesna
- Advantage : as for Aza , probably effective in higher proportion of patients
- Adverse side effects : bone marrow suppression

Mycophenolate

- Initial dose = 500 bid , increase over few weeks to 1500 mg bid
- Maintenance dose = unknown
- Advantage : improves nephritis , better tolerated than cyclophosphamide
- Adverse side effects : diarrhea , nausea , infection , neutropenia , thrombocytopenia

Combination therapy ; AZA + CYC

- Initial dose = 1.5 -2.5 mg / kg / day orally for AZA & 1.5 – 2.5 mg / kg / day orally for CYC
- Maintenance dose = 1-2 mg / kg / day forAZA & 1-2 mg/kg/day for CYC
- Advantage : possiblt more effective than one drug

- Adverse side effects : infections for AZA & Cystitis for CYC

Hemolytic cystitis , urinary bladder sclerosis & carcinoma of the urinary bladder are infrequent if CYC is given intravenously , especially with Mesna

Manifestations of SLE that can be managed with strategies other than OR in addition to immunosuppression

Thrombosis

- Treatment with anticoagulants

Recurrent fetal loss with antiphospholipid

- Heparin in low dose or low-molecular weight heparin with or without aspirin
- If heparin ineffective or not tolerated , use low dose aspirin alone ; GCs plus aspirin in moderate to high dose may be used but is controversial

Thrombocytopenia OR Hemolytic anemia

- Intravenous gamma globulin , splenectomy , Danazol , CYC , Cytotoxic drugs

Seizures without other serious manifestations

- Anticonvulsants

Behavior disorders OR Psychosis without other serious manifestations

- Psychoactive drugs , neuroliptics

Pure membranous glomerulonephritis

- Limited immunosuppressives OR no specific treatment

Section (II)

Guidelines for Differential Diagnosis

Anti-Nuclear Antibodies (ANA)

Is ANA is positive only in SLE :
What other diseases , in which ANA is positive ?
What other diseases , in which ANA is not useful ?

Condition	Patients with ANAs (%)
Diseases for which ANA Testing is helpful for Diagnosis	
SLE	99 – 100
Systemic Sclerosis	97
Polymyositis / Dermatomyositis	40 – 80
Sjogren,s Syndrome	46 – 96
Diseases in which ANAs is required for the Diagnosis	
Drug-induced Lupus	100
MCTD	100
Autoimmune Hepatitis	100
Diseases in which ANAs may be useful for prognosis	
Juvenile RA	20 – 50
Antiphosolipid Antibody Syndrome	40 – 50
Raynaud,s phenomenon	20 – 60
Some diseases in which ANA is typically not useful	
Rheumatic disease	
Discoid Lupus Erythematosis	5 – 25
Fibromyalgia	15 – 25
Rheumatoid Arthritis	30 – 50
Relatives of patients with autoimmune diseases	5 – 25
Multiple sclerosis	25
Idiopathic thrombocytopenic purpura	10 – 30
Thyroid disease	30 – 50

Patients with silicone breast implants	5 – 25
Infectious diseases	Varies widely
Malignancies	Varies widely
Normal persons	
➢ 1 : 40	20 – 30
➢ 1 : 80	10 – 12
➢ 1 : 160	5
➢ 1 : 320	3

Diagnostic characteristics of the ANAs

If ANA is positive with Immunofluorscence , how you can interpret ?
What further tests should be done ?

Interpretation of immunofluorescence patterns & Further studies :

Pattern	It may be	Primary associated rheumatic diseases	Ask for
Rim . Homogeneous	ds-DNA	SLE	RIA , ELISA , CIF , Farr
Rim , homogeneous	ss-DNA	SLE	RIA , ELISA , CIA
Homogeneous , rim	H1 , H2a , H2B , H4	SLE , DIL , RA , PBC , Scl	
Large speckles	H3	SLE , UCTD	
Speckles	Centromere	Scl , SLE , Ss	IF , ELISA
Speckled	Sm	SLE	
Speckled or negative	Ro / SS-A	SS , SCLE , NLE , SLE , PBC , Scl	ID , ELISA ,IB , IPP
Speckled	La / SS-B / Ha	SS , SCLE , NLE ,	ID , ELISA ,IB , IPP

		SLE , DM	
Homogeneous	Mi-2	DM	ID , IPP
Punctate	RNA polymerases (RNAP)		IPP , IB
Nuclealar	RNAP I	Scl	
Nuclealar / Nucleolar	RNAP II	Scl , SLe , overlap	
Nuclealar / Nucleolar	RNAP III	Scl	
Nucleolar , cytoplasmic	Ribosomal RNP	SLE	Id . IB , IPP , ELISA
Diffuse , grainy nuclear / nucleolar	Scl70 (topioisomerase I)	Scl	ID , IB , ELISA
Homogeneous nuclear / nucleolar	PM-Scl (PM-1)	PM , DM , Scl , overlap	ID , IPP , IB
Diffuse	tRNA (Jo-1)	PM , DM	ID , IPP , IB , ELISA , AAI

AAI = aminocylation
CIE = counterimmunoelectrophoresis
CIF = Crithidia Lucilia immunofluorescence
DIL = Drug-induced Lupus
Dm = Dermatomyositis
ELISA = enzymelinkes immunosorbent assay
Farr = Farr radioimmunoassay
IB – immunoblot
ID = immunodiffusion
IPP = immunoprecipitation
MCTD = mixed connective tissue disease
NIL= neonatal lupus erythematosis
Overlap = overlap syndromes
PBC = primry biliary cirrhosis
PM = ploymyositis
RA = rheumatoiod arthritis
RIA = radioimmunoassay
Scl = systemic sclerosis
SCLE = subacute cutaneous lupus erythematosis

SLE = systemic lupus erythematosis
SS = Sjogren,s syndrome
RNA = transfer RNA
UCTD = undifferentiated connective tissue disease

Guidelines for suspicion of ANA diseases :

If you suspect ANA disease :
Obtain Immunofluorescence ANA (FANA)

We have 3 possibilities

1-If negative

Consider :

- Anti-Ro. SS-A … If positive … It may be SLE
- Anti-tRNP synthestases (anti-Jo-1 , etc) … if positive … It may be PM / DM
- Antiphospholipid … if positive … It may be hypercoaguable state

2-If positive with low titer

- Do as if , it is negative (do as before)

3-If it is positive OR low titer but with high suspicion

- If there is skin &/or joint involvement … ask for anti-dsDNA OR anti-Ui snRNP OR anti-Sm OR anti-RO?SS-A … If positive … think about SLE

- If there is drug exposure … ask for antihistone … If positive … think about Drug – induced Lupus

- If there are Raynaud,s , Sclerodactyly , Myositis , Telangiectasiasis , Esophageal dysfunction , Lung disease … ask for anti-Scl 70 , anti-RNA polymerase , anticentromere … If positive … think about Systemic sclerosis

- If there are Raynaud,s , Sclerodactyly , Myositis , Telangiectasiasis , Esophageal dysfunction , Lung disease … ask for anti-U1 snRNP … If positive think about MCTD

- If there are Raynaud,s , Sclerodactyly , Myositis , Telangiectasiasis , Esophageal dysfunction , Lung disease … ask for anti anti-tRNP synthestase (anti-Jo-1 , etc) … If positive think about PM . DM

- If there is sicca syndrome … ask for anti-Ro/SS-A , anti-La/SS-B … if positive … think about Sjogren,s syndrome

Antinuclear Antibodies (ANAs) in SLE

Antibody Specificity	Prevalence (%)
Chromatin-Associated ntigens	
Ds-DNA	73
Histone	50-70
Chromatin	88
Ku	20-40
PCNA	3-6
RNA polymerase II	9-14
kinetochore	6
Ribonucleoproteins	
snRNPs	
Sm core	20-30
U1snRNP	30-40
U2 snRNP	15
U5 snRNP	?
U7snRNP	?
Ro/SS-A	40
La/SS-B	10-15
Ribosomes	
PO , P1 , P2 protein	10-20
28S rRNP	?
S10 protein	?
L5 protein	?
L12 protein	?
proteasome	58

ANA in Sjogren,s Syndrome

Antibody specificity	Prevalence (%)
Ro/SS-A	40-95
La/SS-B	87
Fodrin	64-100
Proteasome	39
MA-1	8
pp75 (Ro-associated protein)	6
Kinetochore	4
p80-collin	4

Guidelines for Arthrocentesis

Indications for Arthrocentesis :

Aspiration of synovial fluid may be indicated in any joint with detectable effusion or may be attempted in joints without detectable effusions when diagnosis is in doubt

1-Undiagnosed Arthritis with Effusion

Characterize type of arthritis

- Non-inflammatory (WBC < 20000 /cmm)
- Inflammatory (WBC > 2000 cmm)
- Septic (WBC > 50.000 / cmm)

Definite Diagnosis

- Gout (urate crystals)
- Pseudogout (CPPD crystals)

Septic arthritis

- Gram stain { rare } or culture

2-Undiagnosed Arthritis without Effusion

May be definitive in gout (knee , 1st MTP joint)

3-Patient with known diagnosis

- Septic arthritis (repeated taps for adequate drainage)
- Other types of arthritis for symptomatic relief (with or without injection) (most studies show improved effect if fluid aspirated before injection)

Therefore you aspirate to characterize the type of arthritis , to confirm diagnosis , OR to drain pus &/or relief symptoms

Guidelines for synovial fluid analysis

Classification according to Synovial fluid White Blood Cell Count

Count = (0 – 200)

- Normal : mainly mononuclear , clear fluid & high viscosity – the amount is small not demonstrable on physical examination

Count = (0 – 2000)

- Osteoarthritis : mainly mononuclear , clear fluid ,& high viscosity – may show cartilage debris
- Structural internal derangement : mainly mononuclear , clear fluid & high viscosity – may show RBC & cartilage debris
- Traumatic : mainly RBCs , cloudy or bloodyfluid & high viscosity – may show high protein content

Count = (2000 – 10000)

- Pigmented villonodular synovitis :main cell content is RBCs , with brown or bloody fluid & low viscosity – high protein content
- Amyloid : mainly mononuclear cells , slightly turbid fluid – use Congo red to confirm
- Enteropathic arthritis : mononuclear & polymorphs , with slightly turbid fluid
- SLE : mainly mononuclear cells , slightly turbid & high viscosity – Low complement

Count = (5000 – 50000)

- Juvenile RA : mainly polymorphs , slightly turbid fluid & low viscosity , low glucose high protein & low complement
- Sarcoidosis : slightly turbid fluid , with low viscosity
- Reiter,s syndrome : mainly polymorphs , slightly turbid fluid with low viscosity , low glucose , high potein & high complement
- Psoriatic arthritis : mainly polymorphs , slightly turbid fluid with low viscosity & low glucose
- RA : mainly polymorphs , turbid fluid & very low viscosity – low glucose & very high protein content
- Tuberculosis arthritis : mainly mononuclear cells , turbid fluid & very low viscosity – very low glucose content & very high protein

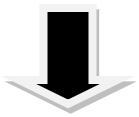
Count = (10000 – 150000)

- CPPD pseudogout : cells mainly polymorphs , turbid fluid & variable viscosity – may show CPPD crystal (in approximately 60%) – low glucose & high protein content
- Gout : mainly polymorphs , turbid fluid & high viscosity – It may show monosodium urate dehydrate crystals (in > 90 %)
- Gonococcal infection : mainly polymorphs , turbid fluid to pus & very low viscosity – very low glucose content & very high protein content - It may show micro-organisms
- Nongonococcal infection : the cells are mainly polymorphs & very turbid fluid up to pus – the glucose content is very low & very high protein content – It may show micro-organisms

Guidelines for Synovial Fluid Analysis in Septic Arthritis

If you suspect a case of septic arthritis
Do diagnostic arthrocentesis
(always try to tap the joint dry)

- Note which joint
- Total volume of synovial fluid
- Gross description of fluid , bloody or non-bloody



If the fluid is bloody
Consider the following differential diagnosis of Hemoarthrosis

- Trauma with or without fracture
- Over anticoagulation
- Hemophilia
- Other bleeding disorders
- Pigmented villonodular synovitis or other tumors
- Traumatic tap

Then consider the WBC count
If it is > 50.000 / cmm
It is markedly inflammatory fluid :
Consider empiric antibiotic therapy pending culture results

If it is < 50.000 / cmm
It is non-inflammatory or moderately inflammatory fluid
Consider a broad differential diagnosis from OA to RA
However , septic arthritis is less likely but still possible

Ten consider crystals ?
Under polarized light microscope

If it is positive
So , it is gout or pseudogout at least
But do also gram stain & culture

If no crystals
Ask for gram stain &/or culture positive
If positive
It is septic arthritis

If it is negative
It means markedly inflammatory fluid due to crystals or infection :
Consider the other possibilities

Guidelines for prescribing TNF-alfa blockers in adults with Rheumatoid arthritis

(Update of previous guidelines of April 2001)

Ledingham & Deighton , on behalf of the British Society for Rheumatology Standards , Guidelines & audit Working Group (SGAWG) . Rheumatology Vol. 44 No. 2 ; P: 157-163 ; 2005

Eligibility for treatment with biologics therapies

Patients must

1- Fulfill the 1987 criteria of the ACR classification criteria for a diagnosis of RA
2- Have active RA (have a DAS28 score of > 5.1) . Measurements of disease activity should be made at two points , 1 month apart confirming on-going active disease
3- Have failed standard therapy as defined by failure to respond or tolerate adequate therapeutic trials of at least two standard DMARDs … IM gold , Hydroxychloroquine , Sulfasalazine , Penicillamine , Azathioprine , Methotrexate or Leflunomide) . One of the failed or not tolerated therapies must be MTX

Adequate therapeutic Trial is defined as :

A- Treatment for at least 6 months , with at least 2 months at a standard target dose unless significant toxicity limited the dose tolerated
B- Treatment for less than 6 months where treatment was withdrawn because of drug intolerance or toxicity , but normally after at least 2 months at therapeutic doses

There may be circumstances when other DMARDs are relatively contraindicated , so that anti-TNF therapy may be considered very early in the course of the disease , & in patients in whom MTX has not been used

Exclusion Criteria

Reference should be made to the individual drug data sheets , but important exclusions include :

1- Women who are pregnant of breast feeding
2- Active infection
3- Septic arthritis of a native joint within the last 12 months (based on opinion , but no good evidence)

4- Sepsis of prosthetic joint within the last 12 months or indefinitely if the joint remains (in situ) (based on opinion , but no good evidence)
5- New York Heart Association (NYHA) grade 3 or 4 congestive cardiac failure (CCF)
6- Clearly history of demyelinating disease

Extreme caution needs to be taken in those patients who are prone to infection e.g.

- Chronic leg ulcer
- Persistent or recurrent chest infection &
- In-dwelling urinary catheters

Criteria for withdrawal of therapy

1- Development of drug-related toxicity
2- Inefficacy as indicated by failure of the DAS28 score to improve by > 1.2 or to reduce to a score of < 3.2 after 3 months of therapy . However if other changes of therapy have occurred within the first 3 months (e.g. the treatment has allowed a reduction in steroid dose) , treatment my be continued for a further 3 months , but should not be maintained for more than 6 months if the DAS28 responss are not achieved (this statement is based on opinion rather than evidence)
3- Severe intercurrent infection (temporary withdrawal)
4- Pregnancy (temporary withdrawal)

Which Anti-TNF therapy should be used ?

- There is no current evidence to suggest that any type of ant-TNF therapy is more efficacious than the other
- Etanercept & adalimumab do not require co-prescription with MTX , so that this is an attractive option in patients intolerant of this drug

Should a patient who is failing to respond to one anti-TNF therapy have their treatment changed to an alternative anti-TNF agent ?

- There are a limited number of studies that have suggested that some patients who have shown no or only a partial response to anti-TNF therapy , can benefit from transferring to an alternative type of anti-TNF therapy

Can DMARDs other than MTX be used in combination with anti-TNF therapies ?

- Some reports suggest combination of infleximab with Leflunomide … efficacios but much side effects

- AZathioprine … in one study (abstract) no evidence

- Although it is not necessary to co-prescribe MTX & etanercept , studies have addressed the possibility that the two together may e more efficacious than the individual agents

Is there a place for alteration in th dose or the frequency of administration of anti-TNF therapy ?

- Some patients who have responded well to anti-TNF therapy may be able to remain with a reduced dose or reduced frequency of treatment , & in the absence of large trials each patient needs to have their regime tailored individually
- In the absence of definitive data , the routine use of regimes which depart from those that are recommended cannot be supported as a general policy , & the majority of patients should stay on the recommended regimes

Potential adverse effects related to anti-TNF therapy & guidance related to these :

1- Serious infections . excluding Tuberculosis (TB)

A number of serious infections including some fatalities have been reported in association with the anti-TNF therapies

Guidelines

- Anti-TNF therapy should not be started in the presence of serious infections
- It should be discontinued … but can be re-continued once the infection has completely resolved
- Until large-scale controlled studies are performed , anti-TNF therapy cannot currently be advised in patients who are HIV positive
- Until definitive data are available , anti-TNF therapy shoulf be avoided in patients with hepatitis B infection

2- Tuberculosis (TB)

There have been a large number of TB reported in association with the use o infliximab … also cases with etanercept

Reactivation of latent TB is highest in the first 12 months of treatment , so particular vigilance is required during this time

Guidelines

- Before starting treatment , all patients should be screened for TB in accordance with the British Thoracic Society (BTS) guidelines
- Active TB should be treated adequately before starting treatment
- Prior to therapy , consideration of prophylactic anti-TB therapy should be given to patients with evidence of potential latent disease (past history of TB treatment or abnormal chest X-ray raising the possibility of TB) after consultation with a local TB specialist
- All patients receiving therapy should be monitored closely for TB
- Patients on anti-TNF therapy who developed symptoms suggestive of TB should receive full anti-TB chemotherapy , but may continue their anti-TNF therapy if it is clinically indicated
- Anti-TNF therapy should only be resumed in accordance with the BTS guidelines & after agreement in collaboration with a TB specialist

3- Surgical procedures

Anti-TNF therapy should be withheld for 2 to 4 weeks prior to major surgical procedures

Treatment may be started post-operatively if there is no evidence of infection & once wound healing is satisfactory (information provided by the drug companies)

4- Vaccination

If live vaccines are required

- they should ideally be given 4 weeks prior to commencing treatment
- Or , 6 months after the last infusion of infliximab
- Or , potentially earlier if risks from not vaccinating are high
- Or , 2-3 weeks after last dose of etanercept (information available from the drug companies

5- Malignancy

There have been number of malignancies including lymphoma , reported from studies

Guidelines

- There is no evidence currently for an increase in risk of solid tumors or lymphproliferative disease with anti-TNF therapies

- Patients should be investigated for potential malignancy if clinically suspected & consideration should be given to stopping anti-TNF treatment if malignancy is confirmed

- Caution should be exercised in the use of anti-TNF therapies in patients with previous malignancy
- If patients have been free of any recurrence of their malignancy for 10 years there is no evidence for a contraindication to anti-TNF therapy

6- Systemic Lupus Erythematosis syndromes & autoimmunity

Rare cases of SLE syndromes have been reported in association with anti-TNF therapies

Symptoms resolved on discontinuing therapy – usually within 6 weeks to 14 months

Guidelines

If symptoms of SLE developed
- Anti-TNF treatment should be discontinued
- Appropriate treatment should be initiated for the clinical symptoms & signs

7- Congestive Cardiac Failure / Cardiovascular disease

Guidelines

- Anti-TNF therapy should not be initiated in patients with New York Heart Association (NYHA) grade 3/4 CCF.
- It should be used in caution in patient with mild CCF
- Patients should be monitored for CCF whilst being treated with any anti-TNF therapy
- If symptoms & signs of CCF are stable , treatment should still potentially be discontinued if the benefit of the anti-TNF therapy is only limited
- It should be discontinued if CCF increases whilst on treatment

8- Demyelination & neurological complications

There are a number of reports of their association with anti-TNF therapy

Guidelines

- It should not be given when there is a clear history of demyelinating disease
- It may be best avoided if there is a possible history of demyelinating disease or a strong family history of demyelination
- It should be withdrawn if demyelination occurs

9- Hematological complication

Pancytopenia was fatal in some patients treated with etanercept & infliximab

Guidelines

- It should be discontinued if haemtological complications arise
- Checking a full blood count periodically , & immediately if the patient is unwell , is recommended

10- Pregnancy & Lactation

There are no data to suggest any risk to the fetus , but insufficient data to warrant continuation of the therapy during pregnancy & information from the drug companies

Guidelines

- Safety of the anti-TNF therapies is unknown / has not been established through pregnancy or lactation

It is recommended that

- Pregnancy should be avoided whilst on anti-TNF therapies & effective contraception is strongly recommended to prevent pregnancy in women of child-bearing potential
- Breastfeeding should be avoided
- Stop it if pregnancy occur
- Infliximab is discontinued for 6 months before a female patient becomes pregnant or a male patient fathers a child … no data for etanercept & 5 months for adalimumab

Dietary supplements

Patients often use dietary supplements or herbal remedies to treat their symptoms . Many adults used herbal medicines along with conventionally prescribed medications . The preponderance of dietary supplements & herbal remedies is a major concern for several reasons :

1- These products are marketed as dietary supplements , not subjected to regulation by authorities & there is no assurance that they contain sufficient quantities of the active ingredients

2- These products are often expensive , which raises the concern that patients well delay necessary treatment

3- These products may interact adversely with the patient,s prescribed medications or have toxicities of their own

Because patients may not disclose their use of alternative therapies , physicians should periodically ask patients about their use of these products

Approach to patients who wish to use dietary supplements OR Herbal Remedies

1- Listen to the patients & provide information
2- Explain that these treatments may help the pain & appear to be safe
3- Have them obtain the supplement from a reputable company & get advice from the pharmacist
4- Inform that these treatments are expensive

5- Do not stop current medications
6- Be observant ; if there is untoward effects , which may be due to the supplement or its interaction with currently prescribed medicines , the patient should contact the physician

7- Do not stop the nonpharmacologic management (e,g. weight reduction , exercise program or physical therapy)
8- Reassess the situation at 3 months , & if there is no noticeable improvement , the supplements can be stopped

Acute Monoarticular Arthritis

Initial approach to monoarticular arthritis

Complaint
Acute joint pain (mono-articular)

Complete history & full examination

First exclude Periarticular Syndrome
(Tendinitis) (Bursitis) (Strain) (Sprain) (Osteomyelitis)
(Soft tissue rheumatism)

If excluded & the patient has true monoartocular arthritis

Ask about significant trauma OR examine for focal bone pain

If yes
Ask for Radiograph

If acute changes … it could be…Fracture or Avulsion
If chronic changes … it could be … OA or CPPD

If there is effusion OR inflammation
Do arthrocentesis & send for Synovial fluid analysis

If Synovial fluid WBC < 1000
It is noninflammatory arthritis (OA , internal derangement)

If Synovial fluid WBC > 5000
It is acute inflammatory arthritis

If Synovial fluid bloody
Do MRI
It may show occult fracture , tumor , internl derangement

If MRI showed nothing
Do Arthroscope which my show internal derangement

If the joint showed no effusion or swelling

Ask for routine laboratory investigations
(include CBC , ESR , CRP , RF , or even ultrasound guided aspiration or CT/MRI)

If all investigations , imaging & full examination reveal nothing except acute arthritis

Give basic therapy
(NSAIDs) (joint protection)
(Observe in frequent visits with short intervals)

Differential Diagnosis of Monoarticular Arthritis

Common causes

1-Causes usually monoarticular

- Septic arthritis
- Crystal diseases (gout & pseudohout)
- Internal derangement
- Ischemic necrosis
- Hemoarthrosis
- Trauma or overuse
- Pauciarticular juvenile rheumatoid arthritis
- Neuropathic
- Congenital hip dysplasia
- Osteochondritis dissecans
- Reflex sympathetic dystrophy syndrome
- Hydroxyapatite deposition
- Loose body
- Palindromic rheumatism
- Paget,s disease
- Stress fracture
- Osteomyelitis
- Osteogenic sarcoma
- Synovial osteochondromatosis

2-Causes usually polyarticular , but may present monoarticular

- RA
- OA
- Psoriatic arthritis
- Reiter,s syndrome
- CPPD
- Chronic articular hemorrhage
- Most JRA & juvenile spondylitis
- Erythema nodosum
- Sarcoidosis
- Serum sickness
- Henoch-Schonlien purpura
- SLE
- Lyme disease
- Dialysis arthropathy
- Other crystal induced arthropathies

- Undifferentiated connective tissue disease

Rare causes

1- Causes usually monoarticular
- Pigmented villonodular synovitis
- Plant thorn synovitis
- Familial mediterranian fever
- Synovioma
- Intermittent hydroarthrosis
- Pancreatic fat necrosis
- Gaucher,s disease
- Behcet,s disease
- Regional migratory osteoporosis
- Giant cell arteritis
- Amyloidosis (myeloma)

2- Causes usually polyarticular & may present monoarticular
- Relapsing polychondritis
- Enteropathic disease
- Hyperlipidemia types II & IV
- Still,s disease
- Pyoderma gangrenosum
- Pulmonary hypertrophic osteoarthropathy
- Chondrocalcinosis-like syndromes
- Rheumatic fever
- Paraneoplastic syndromes

Is the arthritis Acute OR chronic :

- Extremely rapid onset of pain (over seconds or minute) suggests an internal derangement , fracture , trauma or losse body
- Acute onset over several hours to 2 days is typical for most forms of inflammatory arthritis , particularly bacterial infection & crystal induced synovitis

Guideline for Acute Monoarticular Inflammatory Arthritis

If the aspirated synovial fluid , showed WBC count > 5000 / cm3
Do Gram stain

If positive
It is Infection , ask for cultures

If negative
Ask for crystal examination I addition to cultures

If positive for crystals
It could be Gout , CPPD & rule out superinfection

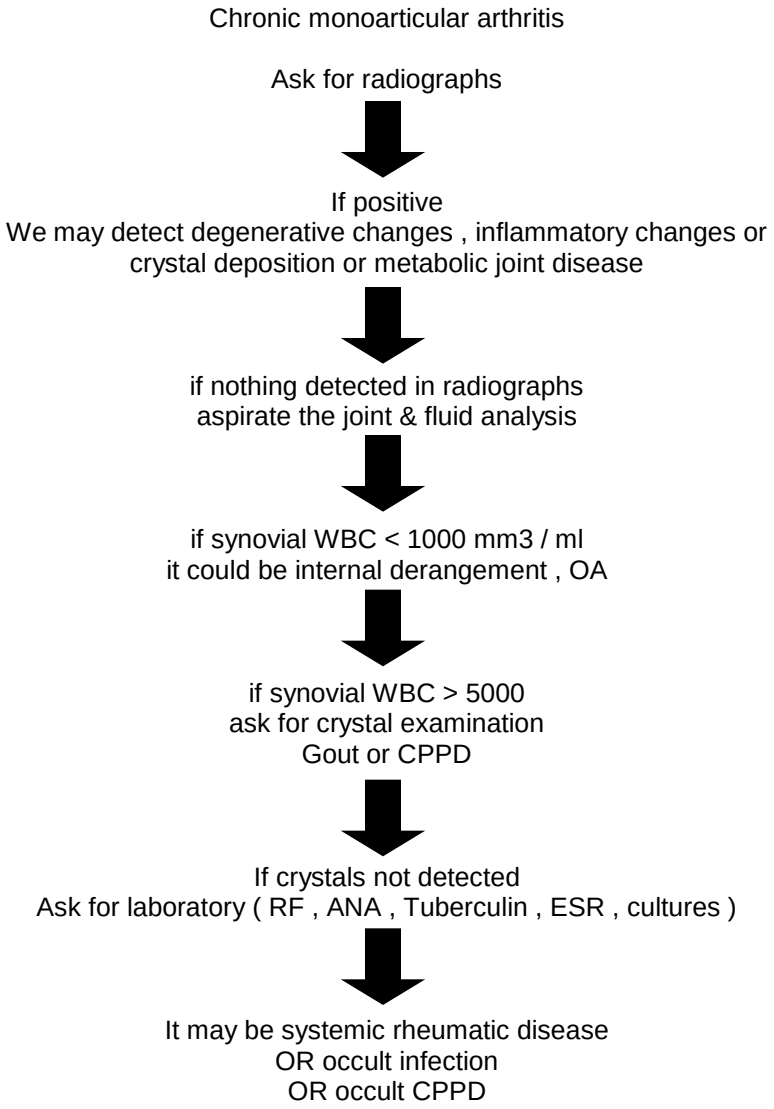
If no crystals
Wait for cultures results (cultures pending) &
Ask for (CBC , ESR , RF , ANA ,)

If results reflect systemic toxicity
Give empiric antibiotics x 24 hours , awaiting cultures

If no systemic toxicity
Think about CPPD , Rective arthritis or systemic rheumatic disease
At that time give
NSAIDs & follow up in 1 to 2 days

If joint worsen , reaspirate

Guideline for Chroic Monoarticular Arthritis



Classification of Polyarthritis

Causes may be inflammatory :

1-Peripheral polyarticular

- RA
- SLE
- Viral arthritis
- Psoriatic arthritis (occasionally)

2-Peripheral pauciarticula

- Psoriatic arthritis
- Reiter,s syndrome
- Rheumatic fever
- Polyarticular Gout
- Enteropathic arthritis
- Behcet,s disease
- Bacterial endocarditis

3-Peripheral with axial involvement

- Ankylosing spondylitis (especially juvenile onset)
- Reiter,s syndrome
- Enteropathic arthritis
- Psoriatic arthritis

Causes , noninflammatory (osteoarthritis)

1-Hereditary

- OA of the hand
- Primary generalized OA

2-Traumatic OA

- OA following local injury
- OA of the knee in obese people
- Condromalacia following aggressive exercise programs
- OA in the elderly

3-Metabolic diseases (may have an unusual pattern)

- Hemochromatosis
- Ochronosis
- Acromegaly

4-Idiopathic

Guidelines for local injection

Indications for Therapeutic Injection

1-Inflammatory Arthritis

- RA : almost always effective , duration varies , should be used as an adjunct to an overall regimen of disease modifying therapy
- Crystal-induced arthritis : few published studies , effective in 24 to 48 hours
- Undiagnosed early inflammatory oligoarthritis : complete response in 2 weeks in57% : predictor of good outcome

- Spondyloarthropathies : peripheral joints respond as in RA .. sacroiliac joint injections under fluoroscopy
- Juvenile RA : particularly useful in oligoarticular form ; may be disease modifying
- Miscellaneous diseases (anecodotal) : Sarcoidosis . Lupus . etc .

2-Non-inflammatory Arthritis

Osteoarthritis :

- Knees : 60 to 80% response in1 to 6 weeks vs placebo : no difference at 12 weeks
- Hips : anecdotal reports ; require fluoroscopy , usually avoided
- Hyaluronic acid derivatives (hyalgan , Syriviscl) weekly for 3 to 5 weeks , moderately better than placebo

Hemophilic arthropathy

- Reported , but rarely used

3-Non-articular Conditions (Tendenitis , bursitis , myofascial pain , etc)

Trigger point injections

- Done frequently
- Not supported by studies

Painful shoulder (Rotator cuff tenditis , Frozen shoulder , etc)

- Efficacy compared to placebo
- Lasting 4 to 6 months

Lateral epicondylitis (Tennis elbow)

- Efficacy for 1 to 2 months vs placebo

Carpal Tunnel Syndrome

- 90% short-termresponse
- Variable at 6 to 12 months
- Good response to injection may be predicator to surgical response

de Quervin,s tenosynovitis

- 70% to 90% improved with 1 to 2 injections
- Relapse in 30% t 1 year

Trochanteric pain of hip

- Bursitis , tendinitis
- 60 to 70% t 6 months (uncontrolled)

Knee pain Syndromes

- Anserine bursitis
- Patellofemoral pain syndromes
- Synovial plica
- Popliteal cyst (usually treated with intra-articular knee injection)

Plantar Fasciitis

- Variably but probably better
- For 1 to 3 months

Morton,s (interdigital) neuroma

- Response often prolonged (no controls)

Tarsal Tunnel Syndrome

- Rarely reported
- Usually only temporary

Achilles Tendenitis & bursitis

- Usually avoided

Cervical girdle , Lumbar areas , posterior hip :

- Uncertain what structures
- Injected without fluoroscope facet block
- Efficacy not proven

Injectable preparations for Intra-articular Injection

Glucocorticoids	Prednisone equivalent
Betamethazone sodium phosphate (6 mg / ml)	
Dexamethazone sodium (4 mg / ml)	
Dexamethazone acetate (8 mg / ml)	
Hydrocortisone acetate (24mg/ml)	
Methylprednisolone acetate (40mg/ml)	
Prednisolone terbutate (20mg/ml)	
Triamcinolone acetanoids (40mg/ml)	
Triamcinolone hexacetonide (20mg/ml)	
Hyaluronic acid • Weekly for 3 to 5 weeks • Indicated in OA of knee	
Hyalgan (20 mg / 2ml)	
Syrvisc (16mg/2ml)	

The originally injected hydroxycortisone acetate is still available , widely used & inexpensive

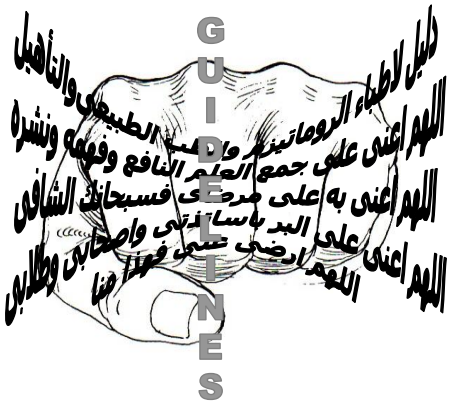
Triamcinolone hexaacetonide is one of the least soluble agents with the presumed most-prolonged effect

Steroid preparations are often mixed with local anaesthetics , particularly for injecting small joints , tendon sheaths & periarticular structures . This serve to reduce the local discomfort of injection into a confined space & also dilutes the concentration of the locally injected steroid & reduces the risk of soft tissue atrophy .

Guidelines for the dosage of steroid injected into given joints is based on the size of the joint injected
Although no consensus exists regarding these amounts , most experts suggest injecting 1 ml of steroid preparation into large joints, smaller amounts into smaller joints

الدليل

لعلاج بعض امراض الروماتيزم



صفوت العربى
استاذ امراض المفاصل والروماتيزم
كلية الطب – جامعة الازهر
القاهرة - مصر

بسم الله الرحمن الرحيم

الزميل العزيز
طبيب الروماتيزم

فى هذا الكتيب وبمناسبة انعقاد المؤتمر الاول لاقسام الروماتيزم بجامعة الازهر .. حاولت ان اجعله دليلا لك لتشخيص وعلاج بعض امراض ومشاكل عالم الروماتيزم وما اكثرها على ان تكون ذات توثيق وموافقة عالمية او لهيئة دولية او باحد امهات مراجع الروماتيزم .

ما دفعنى الى هذا الجمع هو حاجتنا المستمرة والكثيرة وخاصة لاطبائنا الجدد الى خطوط علاجية واضحة .. وبدائلها عند الحاجة .. حتى تعيننا على حل الغاز هذا العلم الواسع والعميق والذى يتصل ويتداخل مع كل فروع الطب الاخرى ... ولاشك انك تتفق معى فى انه لا يوجد فرع من فروع الطب او جهاز من اجهزة البدن الا ويتداخل مع امراضنا وتكون اصابته احد اعراض امراضنا او احد مضاعفاتها

اذا تعالى معى ولنتجول من خلال سطور هذا الكتاب ولنطلع على بعض الادلة او المناهج والتى كثيرا ما تكون حديثة واحيانا ما تكون قديمة نوعا ولكن لم يأتى ما يلغيها ... ولنضع هذه المناهج او الادلة امام اعيننا لتكون نبراسا لنا فى علاج مرضانا

ولا يفوتنى ان شأ الله ان اتقدم بخالص الشكر والتقدير لزملائى الاعزاء والافاضل على ما بذلوه من جهد وسعى لاخراج هذا الدليل بصورة ان شأ الله نافعة لزملاءنا الاطباء وبالتالى يأتى النفع على مرضانا شفاهم الله ... ولا املك لهم الا الاحترام والتقدير والدعاء لهم بكل الخير والتوفيق والفلاح وان يجزيهم الله كل الخير على ما قدموه ... وستجد اسماء هؤلاء العلماء الافاضل كمشاركين فى الجهة الاخرى من الكتاب

والحمد لله رب العالمين

المحرر
صفوت العربى

الدليل الاول

حار عقلى وجنانى بحثا عن دليل اتوجه به الى زملائى اطباء الروماتيزم كدليل اول يعيننى واياهم على علاج مرضانا ... ثم تعجبت لنفسى كيف لى ان اغفل عن قول الحق سبحانه وتعالى فى سورة الاعراف (الاية: **36**) (وكلوا واشربوا ولا تسرفوا) .. فقد قيل ان الله جل شأنه قد ذكر الطب فى نصف اية

ولزميلى الفاضل ومن وحى هذه الاية الكريمة , اقدم لك الدليل الاول :

اسئل مريضك دائما بالاعتدال فى كل شىء

اسئله الاعتدال فى الطعام ... فلا يسرف فى الاكل ... وحدث ولا حرج عن اضرار ومشاكل الاسراف فى الطعام ولكن ما يخصنا فى الامر هو العداوة الشديدة بين السمنة والجهاز الحركى ... اسئله الا يسرف فى الصيام لان الجهاز الحركى فى حالة احلال وتجديد مستمر ودائم حتى النهاية , لذا يجب ان نمد انسجته بالطعام الجيد والطيب حتى يؤدى وظيفته على اكمل وجه

واسئله الاعتدال فى الحركة ... فلا يسرف فى الراحة , فقد خلق الله جهازه الحركى للحركة والنشاط , فهكذا ينمو وهكذا يصلح ويعمل بكفاءة وهكذا يتجدد ... ولا يسرف فى الحركة , فربما يزيد معدل الاستهلاك عن امكانياته

انصحه بالا ينام كثيرا ... وانصحه بالا يسهر كثيرا
انصحه بالا يجلس كثيرا ... والا يقف لفترات طويله

حتى العبادات (وهى ما خُلقنا لاجلها), نصحنا نبينا الكريم (صلى الله عليه وسلم) الا نسرف فيها , فقد قال لمن يقيم الليل ولا ينام ولمن يصوم الدهر ولا يفطر ولمن يعتزل النساء ... انه خير منهم (وهذ حق) وهو يقيم الليل وينام ويصوم ويفطر ويتزوج النساء .

قال رسول الله صلى الله عليه وسلم (يايها الناس عليكم من الاعمال ما تطيقون فان الله لا يمل حتى تملوا وان احب الاعمال الى الله ما دووم عليها وان قل)

كما قال (ان الرفق لا يكون فى شىء الا زانه ولا ينزع من شىء الا شانه)

الدليل الثانى

وليكن دليلنا الثانى هو حديث سيد الانام (صلى الله عليه وسلم)
(يا عباد الله تداووا , فان الله لم ينزل داء الا انزل له شفاء , عَلِمه من علمه وجَهِله من جهله) (رواه مسلم)
وقال (لكل داء دواء , فاذا اصيب دواء الداء , برأ باذن الله عز وجل) (رواه مسلم)

وها هو نبراسنا الثانى , قد وضعه لنا نبينا الكريم ... فلا يكفينا ان نكون اطباء حتى نعالج الناس , لابد ان نعلم

لا سبيل للعلم الا بالقراءة والاطلاع والاستماع ... ابحث واسئل وتساءل وسجل ماترى وما تسمع .. واحرص على حضور اللقاءات العلمية والندوات والمؤتمرات ... ولا يكن حضورك سلبيا .. احرص على المشاركة ولا تستحى من السؤال عما تجهل (تذكر انك اذا استحيت من السؤال سيكون خجلك اكبر امام مريض تجهل مرضه او علاجه)

لا تفرق فى القراءة بين كتاب وبحث ومجلة ودورية , فستجد لا شك ما يضاف الى علمك وما ينفع مريضك

اسمع اكثر مما تتكلم ... اسمع مريضك واسمع زميلك واستمع جيدا الى محاضرك .. فلا شك فى ان لديه ما يقوله لك وقد بذل الجهد فى اعداده

اذا لم تجد ***من*** تسمعه او لم تجد ***ما*** تسمعه , فلا تنتظر وابحث عنه واسعى اليه ... لا تنتظر الماء من المطر فقد لا يسقط المطر هذا العام ولا الذى يليه وربما لا يسقط حتى تفنى ... اذا ابحث انت تحت الارض وفى الابار

درب ذهنك على تسجيل ما تسمع وتقرأ وترى ... فان لم تسعفك ذاكرتك فسجل فى مفكرتك وليكن لك ارشيفك الخاص لانك لاشك راجع اليه

لا تجعل حضورك مجالس العلم اختيارية ... عملك الحقيقى هو تحصيل العلم والمعرفة والخبرة والمهارة لتنفع بهم مرضاك .. فهم فى حاجة الى هذا العلم اكثر منك ... اذا الامر اجبارى ولا تناقشه بينك وبين نفسك ... اذا سمعت نداء العلم وجب عليك كطبيب الاجابة فما اجمل ان يجبرك طموحك على تحصيل العلم

والان ننتقل الى الحديث الثانى ... وهو تكملة منطقية للمعنى الاول ... فالداء موجود والدواء موجود باذن الله .. وهذا الدواء يعلمه البعض ويجهله البعض وان الشفاء لا يتم الا اذا اصاب الدواء الداء ... اذا فقد علق النبى الكريم الشفاء على ان يصيب الدواء الداء وهذا قدر زائد من الله ... وفى تصورى ان هذا لايحدث الا مع الطبيب الحاذق الشاطر الخبير المطلع الممارس

لا تتصور يا زميلى العزيز ان الامر عشوائى .. وان تحدثك نفسك بان الطبيب الذى يحاول بهذا ويجرب هذا ربما يفلح معه الامر بتوفيق من الله ... بالله عليك كيف يوفقه الله وهو لم يسعى لمعرفة الصواب ويجرب امرا يتعلق بصحة انسان او ربما بحياته ... واعلم ان الامر اذا نجح مرة فليس معنى ذلك انه القاعدة فربما كان هذا التوفيق رحمة من الله لهذا المريض الذى بين يديه ... وحتى اذا كان الامر مصادفة احيانا فان الصدفة لا تأتى الا لمن يستحقها .. ومن يستحقها هو الساعى الى العلم

زميلى العزيز , فى تصورى ان العظماء من الاطباء لم يصلوا الى ما وصلوا اليه بالحظ والعشوائية ولا حتى بالعبقرية (العبقرية لا تأتى بالعلم فالعلم موجود ولكن العبقرية هى كيفية الاستفادة من العلم وتطبيقه) ... بل بالعمل والجهد والصبر والمثابرة والكد والعرق ولقد علم هؤلاء الاطباء الافاضل علم اليقين ... ان ناموس الله فى الارض .. ان لكل مجتهد نصيب وان الله لا يضيع اجر من احسن عملا حتى لغير المؤمنين فهذا الامر للناس كافة ... فقد اجرهم الله على كدهم بالتوفيق مع مرضاهم ... اذا فسر عبقريتهم هو عملهم وجهدهم ... هذا الجهد الذى جعلهم اصحاب بصر وبصيرة .. بصر ليروا ما لا يراه الكسالة من الاطباء وبصيرة ليدركوا ما لا يدركه الادعياء ... وليكن هذا هو سر عبقريتك انت ايضا .. وصدقنى انه امر قريب لو اردت .

اذا اردت ان ترمى فتصيب , فاعد ذراعك بالقوة .. واعد عينيك بحسن الرؤية .. واعد قوسك بحسن الاختيار والتطوير .. واحسن صنع سهامك .... عندئذ سيصيب السهم المرض فى مقتل لا محالة ... اعد نفسك جيدا ولا تنتظر اجرا او شكرا على اعدادك , فان ما ستشعر به حين تصيب سهامك امراض مرضاك سُينسيك هذا تعبك وسيُغنيك عن اى مقابل وهذه المشاعر مقابل ومنة من الله لا يدركها الا من ذاق حلاوتها .. وارجو الله الا يحرمك منها لانك اذا ذقتها , قضيت ليلك فى الاطلاع ونهارك فى علاج مرضاك او تعليم طلابك

الدليل الثالث

ستتعجب ايها الزميل العزيز .. حين تعرف ان دليللنا الثالث يرجع الى سبعة قرون سابقة ولم يضعه لنا احد اطباء او علماء الحضارة الغربية التى نعيش تحت مظلة اكتشافاتها وعلومها الان ولكن وضعه احد اجدادنا العلماء ايام قمة الحضارة الاسلامية وهو العالم والامام شمس الدين ابن قيم الجوزية (**691** : **751** هجرية) ولا تتسرع فى الحكم على الامر وانظر الى اى مدى استطاع هذا الرجل ان ينفذ الى عقول وقلوب الاطباء

ساعرض عليك كلامه دون ادنى تدخل بشرح او تعليق لترى بنفسك عبقرية الرجل وفهمه العميق ... ولو كان الامر بيدى لطلبت من كل طبيب ان يقرأ هذا الدليل يوميا قبل ان يدخل عيادته او مشفاه ... وجزاه الله عنا احسن الجزاء ورحمه رحمة واسعة ان شأ الله

من كلام الامام شمس الدين محمد بن ابى بكر ابن قيم الجوزية (القرن **14** ميلادى)

الطبيب الحاذق : هو الذى يراعى فى علاجه عشرين امرا ك

احدهما :
النظر فى نوع المرض – من اى الامراض هو ؟

الثانى :
النظر فى سببه – من اى شيء حدث , والعلة الفاعلة التى كانت سبب حدوثه – ما هى ؟

الثالث :
قوة المريض , وهل هى مقاومة للمرض او اضعف منه
فان كانت مقاومة للمرض , مستظهره عليه , تركها والمرض .. ولم يحرك بالدواء ساكنا

الرابع :
مزاج البدن الطبيعى ما هو ؟

الخامس :
المزاج الحادث غير المجرى الطبيعى

السادس :
سن المريض

السابع :
عادته

الثامن :
الوقت الحاضر من فصول السنة وما يليق به

التاسع :
بلد المريض وتربيته

العاشر :
حال الهواء فى وقت المرض

الحادى عشر
النظر فى الدواء المضاد لتلك العلة

الثانى عشر :
النظر فى قوة الدواء ودرجته , والموازنة بينه وبين قوة المريض

الثالث عشر :
الا يكون كل قصده اذالة العلة فقط ... بل اذالتها على وجه يأمن معه حدوث اصعب منها ... فمتى كان اذالتها لا يأمن معها حدوث علة اخرى اصعب منها ... ابقاها على حالها ... وتلطيفها هو الواجب

الرابع عشر :
ان يعالج بالاسهل فالاسهل ... فلا ينتقل من العلاج بالغذاء الى الدواء الا عند تعذره ... ولا ينتقل الى الدواء المركب الا عند تعذر الدواء البسيط ... فمن حذق الطبيب علاجه بالاغذية بدل الادوية ... وبالادوية البسيطة بدل المركبة

الخامس عشر :
ان ينظر فى العلة , هل يمكن علاجها او لا ؟

فان لم يمكن علاجها , حفظ صنعته وحرمته , ولا يحمله الطمع على علاج لا يفيد شيئا .
وان امكن علاجها , نظر هل يمكن زوالها ام لا ؟
فان علم انه لا يمكن زوالها , نظر هل يمكن تخفيفها وتقليلها ام لا ؟
فان لم يمكن تخفيفها وتقليلها وراى ان غاية الامكان ايقافها وقطع زيادتها , قصد بالعلاج ذلك , واعان القوة واضعف المادة

السادس عشر :
الا يتعرض للخلط قبل نضجه با ستفراغ , بل يقصد انضاجه , فاذا تم نضجه , بادر الى استفراغه

السابع عشر :
ان يكون له خبرة باعتلال القلوب والارواح وادويتها , وذلك اصل عظيم فى علاج الابدان
فان انفعال البدن وطبيعته عن النفس والقلب امر مشهود .

والطبيب اذا كان عارفا بأمراض القلب والروح وعلاجهما , كان هو الطبيب الكامل ,
والذى لا خبرة له بذلك وان كان حاذقا فى علاج الطبيعة واحوال البدن نصف طبيب
وكل طبيب لا يداوى العليل , بتفقد قلبه وصلاحه وتقوية روحه وقواه بالصدقة وفعل الخير والاحسان والاقبال على الله فليس بطبيب ... بل متطبب قاصر

ومن اعظم علاجات المرض فعل الخير والاحسان والذكر والدعاء والتضرع والابتهال الى الله والتوبة
ولهذه الامور تأثير فى دفع العلل وحصول الشفاء اعظم من الادوية الطبيعية , ولكن بحسب استعداد النفس وقبولها وعقيدتها فى ذلك ونفعه

الثامن عشر :
التلطف مع المريض والرفق به , كالتلطف بالصبى

التاسع عشر :
ان يستعمل انواع العلاجات الطبيعية والالهية , والعلاج بالتخييل , فان لحذاق الاطباء فى التخييل امورا عجيبة لا يصل اليها الدواء , فالطبيب الحاذق يستعين على المرض بكل معين

العشرون :
وهو ملاك امر الطبيب , ان يجعل علاجه وتدبيره دائرا على خمسة اركان :

1 - حفظ الحة الموجودة
2 - رد الصحة المفقودة بحسب الامكان
3 - اذالة العلة اة تقليلها بحسب الامكان
4 - احتمال ادنى المفسدتين لاذالة اعظمهما
5 - تفويت ادنى المصلحتين لتحصيل اعظمهما

فعلى هذه الاصول الخمسة مدار العلاج
وكل طبيب لا تكون هذه اخيته التى يرجع اليها , فليس بطبيب والله اعلم

انظر معى ايها الزميل العزيز لهذا الامام العالم الفاضل وكيف وضع لنااسس ومناهج نسير عليها ونبراسا نهتدى بنوره لعلاج مرضانا انطلاقا من ايمانه وورعه ثم من علمه وخبرته . ولو طبقت هذا الامر على نفسى

- لاجتهدت كثيرا فى الاطلاع وزيادة رصيدى من فنون الطب
- لاجتهدت كثيرا مع مريضى ... لافهم علته ومكنون مرضه
- لاجتهدت كثيرا فى فحص مريضى ... لاتيقن من علته وتقدير درجتها
- لاجتهدت كثيرا فى وصف ما يصلح له من دواء
- لاجتهدت كثيرا فى اعلامه
- لاجتهدت كثيرا فى كسب وده وشحذ همته واثارة عزيمته على الشفاء
- لاجتهدت كثيرا لاخراج مكنون قوى المريض التى وضعها الله داخله ولا يعرف المريض سبيلا لاخراجها الا بمعاونة طبيبه

زميلى العزيز
بالله عليك بعد ان قرأت هذا المنهج للطبيب الحاذق ... اهناك من قرأت له او سمعت عنه استطاع ان يجمع كل هذا المناهج فى دليل واحد
لو كانت لديك اى مشورة او دليل او منهاج فلا تتردد فى الاتصال بى , لننشره سويا على زملاءنا .. مهما كان كاتبه او جامعه .. فقد أمرنا ان نأخذ الحكمة من اى وعاء

الدليل الرابع

هو ان تضع لنفسك دليل خاص
هو ان تضع لنفسك خطوط لمنهج يتناسب مع شخصك , علمك , مشفاك , عيادتك , مرضاك , بلدتك , اجهزتك , الادوية المتوفرة حولك ولديك .. والتى يجب ان تتابع امرها اولا باول حتى لو اضطررت الى سؤال الصيدلية المجاورة

ابدأ خطوط هذا المنهج باكثر الامراض التى تعرض عليك فى موقعك (وليكن مثلا الم اسفل الظهر او خشونة الركبتين)

- اجمع اكبر قدر ممكن من المصادر العلمية والتى تخص هذا المرض
- اطلع على القديم منها والحديث
- رتب فى ذهنك خطوات مسلسلة من لحظة شكوى المريض حتى انصرافه من امامك

ولنبدأ بتاريخ المرض

- ابدأ بوضع الاسئلة التى سوف توجهها الى مريضك بمجرد سماع الشكوى ... الافضل ان تكتبها ... واستعن بما تقرأ من مراجع على وضع هذه الاسئلة مع شيء من التصريف والتعديل حسب الحالة وسنها وظروف عملها

- يجب ان تقرأ هذه الاسئلة عدة مرات وتكررها حتى يستحضرها ذهنك امام المريض ... يجب ان تتعلم لغة الحوار مع المريض حتى تستخرج المفيد من شكواه ... ان لم تجد من يعلمك ... فابحث عنه ... فان لم تجد فعلم نفسك ... فان لم تستطع فاترك مهنة الطب

- علم نفسك بان تُجرى الحوار بينك وبين نفسك ... اسئل السؤال واجب عليه ... اجب مرة بنعم ومرة بلا ... وانظر مع نفسك اذا كانت الاجابة بنعم فماذا سيكون السؤال التالى ... واذا كانت بلا فماذا سيكون السؤال عندئذ ... وهكذا دع الحوار يتشعب منك ولكن احذر ان تخرج بالحوار عن خط عام تحدده انت

- لكل حوار ادواته ... وادوات حوارك هى مجموعة من الاسئلة يجب ان تستوفى نقاطها مع مريضك بحيث يمكنك ان تصل لتشخيص مبدئى وتقييم قبل ان تصل للفحص

ولننتقل للفحص

- يجب ان تكون لديك خطة للفحص ولاتترك الامر عشوائيا

- يجب ان يكون لديك عدة اختبارات لكل مفصل يجب ان تجريها على المريض مع شىء من التعديل لكل حالة

- اكتب هذه الاختبارات وكرر قراءتها حتى يستحضرها ذهنك عند فحص المريض ولاتمل ولاتيئس وكرر الامر عشرات المرات حتى على نفسك حتى تحفظها عن ظهر قلب ... فهذه هى ادواتك التى سوف تستعملها مدى حياتك العملية مع شىء من التطوير مع الوقت ... اذا الا يستحق الامر ان تجيدها وتصقلها باستمرار حتى تؤديها على اكمل وجه وبصورة الية ... واصدقك القول ان المريض ربما يحكم عليك ويزن قدرك بجودة فحصك ... اذا احسن فحصك لتصل الى التشخيص ولتكسب ثقة مريضك وهذا ايضا ركن هام فى نجاح العلاج

- درب يديك على فحص المفاصل وانت مغمض العينين ... حتى تُحيى بصيرة يديك (درب يديك على ان ترى ما لا تراه العين او تؤكد ما تراه العين) ... جرب هذا الامر على مفاصلك انت حتى تتعرف يديك على العلامات التشريحية للمفاصل والعظام ... ضع لنفسك مقاييس خاصة وابعاد خاصة ... درب يديك مثلا على الفرق بين الصلب واللدن واللين والكيسى او المائى .

التسجيل

- بعد ان تفحص مريضك ... سجل ما وجدته وبكل دقة وتعود الا تتأثر بتشخيص سابق ... سجل الموجود بكل حيدة وضع لنفسك علامات خاصة للتقييم واعطاء الدرجات لان هذا سينفعك فى المتابعة ... طبعا هناك درجات للتقييم عالمية يجب ان نلتزم بها لانها تطبق على مستوى العالم ولكن ما قصدته هو مصطلحات خاصة للتعبير عن الورم مثلا بحرف ما او ما شابه

- من الافضل كثيرا مع نقص امكانيات بلادنا ان نجعل لكل مريض ورقة نكتب فيها ما اتفقنا عليه وهذا الامر ضرورى فى عالم الروماتيزم خاصة لان الكثير من امراضنا مزمنة او راجعة او لفافة ... هذه الورقة يمكن ان تكون الوصفة الطبية نفسها (الروشته) او ورقة من مفكرة تضعها امامك بتاريخ ما او اكون طماع واطلب منك ورقة مطبوعة ومقسمة بمعرفتك انت بها مكان لتاريخ المرض ونتيجة الفحص ونتائج المعمل والاشعة ومكان اخير نكتب فيه ما وصفناه من علاج ومتابعة

التحاليل والاشعة

- ضع خطة ابحاث لكل مرض ... طبعا مع شىء من التصريف لكل حالة ... اذا كان تشخيصى المبدئى (بعد قصة المرض والفحص) هو كذا فسوف اطلب التحليل كذا او الاشعة كذا وهكذا

العلاج

- بعد الاطلاع على نتيجة التحاليل والاشعة والوصول الى التشخيص النهائى ... ضع خطوط عامة للعلاج لكل مرض ... وهذا الامر ليس بجديد , ففى كتابك هذا ادلة لعدة امراض وضعتها هيئات علمية دولية شديدة الدقة ليسير على نهجها الاطباء فى جميع انحاء العالم , فلا ضير ان تستعين بها لوضع ما يخص حالاتك فلربما لا يتوفر لك كل ما تنصح به هذه الادلة

- لا تُخضع العلاج لحالتك المزاجية ... حاول ان تستوفى كل الخطوط مع كل المرضى ... وهذا من اهم فوائد الادلة الموضعة مسبقا , حيث انها وضعت فى ظروف لا تسمح بالكثير من الاخطاء ... لذلك ضع خطوط علاجك لكل مرضاك ان امكن وسر على نهجها

- اكتب دليل للادوية خاص بك حسبما يتوفر لك ولمريضك ... ولا تتردد فى الاطلاع عليه باستمرار وعلى فترات متقاربة فلا احد فوق النسيان الا الله سبحانه وتعالى ... ولا تتردد فى كتابة الجرعات فى هذا الدليل

- لا تنسى وانت تكتب خطوط علاجك اننا نتعامل مع الجهاز الحركى وان الجهاز الحركى دائم الاستعمال وان علاجنا يشمل الدواء والطب الطبيعى والذى يجب ان تذكره تفصيلا فى المخطوط الخاص بك ولا تستحى فى السؤال عن خبرة من

سبقك حتى تجمع الخبرة الخاصة بك ... ثم ننتقل الى الركن الثالث فى علاجنا وهو :

- اعلام المريض بمرضه والتعليمات الخاصة بالاستعمال ... (وتذكر اننا نولد وليس لدينا كاتالوج مكتوب لكيفية استعمال جهازنا الحركى وان هذا الامر فطريا وان فطرتنا قد قتلتها المدنية الحديثة فلا تنسى ان تحييها فى مريضك وعلمه ما يجهله عن بدنه .. وقبل ذلك زد انت من حصيلتك فى هذا الامر)

المتابعة

- ضع ايضا خطة بسيطة للمراجعة ولتكن اسئلة مباشرة وسابقة الاعداد وفحص سريع ومباشر للمفاصل المصابة ... كما يجب اعداد التحاليل اللازمة للتقييم

- ضع لنفسك مقاييس للتقييم واستعن بما هو موجود ... ثم ضع مستويات للعلاج , متى اخفضه ومتى اغيره ومتى استمر عليه كما هو

لا تكتفى بما ذكرته لك .. اضف نفسك الى منهجك

لا تنظر لما ذكرته لك على انه صعب او غير قابل للتطبيق العملى ... لو تدربت عليه جيدا لن يستغرق منك الامر الا **10** دقائق او اكثر قليلا ... طبعا سيستغرق الام مدة اطول فى بداية تطبيقه -- فاصبر قليلا تنعم كثيرا

اذا استطعت ان تضع منهاجا جيدا لاحد الامراض وتدربت عليه ... ستجد الامر ابسط واسهل كثيرا مع المرض الثانى ... وستجده بلا جهد وممتع فى المرة الثالثة ... وستحترفه فى المرة التالية

كلما اكثرت من المناهج التى لديك , كلما سهلت الامر على نفسك وارتحت وارحت مرضاك واتقيت الله فى خلق الله

الدليل الخامس

- اكتب التعليمات الخاصة بكل مرض من نصائح وتعليمات ومسموحات ونواهى حتى تعطيها لكل مريض حسب مرضه واستعن بالمراجع فستجد فيها كل هذه التعليمات
- اذا كان الامر مكلفا .. اكتبها انت لنفسك حتى تبلغها لمرضاك

- اذا تعذر ذلك لضييق وقتك .. فكلف مساعدك

- هذه التعليمات ربما تكون احيانا اهم من الدواء ... ربما ينسى المريضان يسئلك عنها ... ربما يستحى

- ضعها على شريط فيديو واعرضها لكل المرضى بالعيادة

- رتب الى لقاءات علمية بعيادتك واجلس مع مرضاك للمناقشة والاستفسار كل فترة (ولو مرو كل شهر , كل **3** شهور او حتى كل سنة , المهم ان تعقد ويكون هناك حس اجتماعى)

- ضع صور توضيحية وتعليمية بمكان جلوس المرضى ... على ان تكون حسنة التصوير وبصورة محببة ... مثل الوضع السليم للجلوس او حمل الاشياء

- الاتفاق مع اخصائى العلاج الطبيعى على توصيل معلومات ما اثناء جلسات العلاج الطبيعى ... فالمريض يقضى وقت طويل داخل حجرة العلاج الطبيعى وهو فى حالة استرخاء و يمكن استغلال هذا الموقف بما يعود عليه بالفائدة

الدليل السادس

- اجعل لنفسك قضية خاصة فى عالم الروماتيزم
- اجعل لنفسك مرض خاص يحوز اهتمامك
- اقرأ كل شيء او اى شيء عنه
- كن خبيرا فى هذا الامر او هذه القضية او هذا المرض
- سجل مرضاك من هذا المرض بصورة خاصة ولتكن اكثر تفصيلا عن غيره من الامراض
- ابحث دائما عن الجديد فى هذه القضية و اسعى اليه
- اذا لم تحقق شيء ... فلا تيئس وابحث عن قضية اخرى ... عندما يفشل الفارس الحقيقى فى ركوب جواد ما .. فانه يدعه و يبحث عن جواد اخر ويظل هكذا ينتقل من جواد الى اخر ولا يستطيع ان يحيا بلا جواد ... الاجياد كثيرة ولكن الندرة فى الفرسان
- لقد قال رسول الله صلى الله عليه وسلم (بلغوا عنى ولو اية) ... انظر انت لنفسك ... الا تجد نصيحة او معلومة او توجيه ما نتيجة خبراتك الطويلة مع مرضاك
- الم يلفت نظرك شيء ما يستحق منك المتابعة حتى تصل فيه الى رأى تنقله الى من بعدك
- الا تدرى ان الطب كله ما كان فى بدايته الا مجموعة من الخبرات تتناقلها الاجيال .. وان اختلف الامر الان ولابد من دليل لكل راى او توجيه .. والدليل لا يأتى الا بالدراسة
- انظر معى لبعض اقوال الاطباء القدامة والتى رصدوا بها الكثير من النصائح والتى لاذال بعضها سارى حيى الان ... قال الحارث بن كلدة بعد ان سُئل عن الدواء : مالزمتك الصحة فاجتنبه – فان هاج داء فاحسمه بما يردعه قبل استحكامه وقيل استفحاله _ وهكذا استطاع الحارث بدقة ملاحظته ان يأتى بقول يتفق الان مع احدث طرق العلاج
- **Treatment before inflammatory cell expansion**
- والان لاتردد فى ان تضيف قاعدة او ملاحظة او نصيحة او كلمة او حرف فى جملة مفيدة مع زملائك ... فمن غير المعقول ان تأتى السالدنيا وتعمل فى الطب وتكتسب كل هذه الخبرات وترى كل هذه الامراض دون ان تترك كلمة او نصيحة لمن بعدك ... فانت لست اقل ممن قال ولكنك ان لم تفعل فانت اكسل او متطفل على نصائح وخبرات غيرك .

الدليل السابع

- انت ربان سفينة العلاج
- درب نفسك على قيادة هذه السفينة
- اعد ادوات القيادة جيدا
- مرضاك معك فى هذه السفينة
- العلم هو اساس القيادة
- لا تلقى بمرضاك من السفينة (من يأس او نفاذ صبر) فقد يلقى بك طبيبك حين تمرض ولا يوجد من هو معصوم من مرض الا الله جل شأنه
- اصلح سفينتك باستمرار ورمم عيوبها بالاطلاع واكتساب الخبرات

- اذا لم تستطع ان تنقل مريض الى بر الشفاء فلا تستحى من ان تنقله الى سفينة اخرى بها ربانا اكثر منك خبرة بل ساعده على الاختيار ووجهه الى الصواب... لو فعلت هذا لكنت اكثر منه خيرا وحكمة

- لا تعاند ولا تستحى ولا تكابر .. فتغرق السفينة ويغرق مرضاك وانت سابقهم واعلم انك فى علاج مرضاك ضامنا

والان وقد اكرمنى الله بكتابة هذه الادلة السبعة ... عليك ان تنتقل الان الى الادلة الخاصة بكل مرض فى الجانب الاخر من الكتاب ... وقبل ان اتركك ادعو الله كل صباح ان يعينك على مرضاك

والحمد لله رب العالمين

صفوت العربى